```
=> b hcaplus
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FILE COVERS 1907 - 16 Sep 2004  VOL 141 ISS 12
FILE LAST UPDATED: 15 Sep 2004  (20040915/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que l10
L5            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("ALVIS M"/AU OR "ALVIS M
                R"/AU)
L7            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "BROWN MELISSA K C"/AU
L8            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  FIEBIGER R/AU
L10           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 OR L7 OR L8


=> d ibib abs l10 1-5

L10  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1999:358487  HCAPLUS
DOCUMENT NUMBER:          131:120815
TITLE:                    Biocompatibility and degradation of collagen bone
                          anchors in a rabbit model
AUTHOR(S):                Schroeder, Jacqueline A.; Brown, Melissa K. C.
CORPORATE SOURCE:         Cohesion Technologies, Inc., Palo Alto, CA, USA
SOURCE:                   Journal of Biomedical Materials Research (1999),
                          48(3), 309-314
                          CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER:                John Wiley & Sons, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    Bone anchors are used to fasten tendons and ligaments to bone during
      reconstructive surgery. Although metal anchors are often used, an anchor
      that could resorb and permit normal bone regeneration would be
      advantageous. The objective of the study was to evaluate the
      biocompatibility and degradation of bone anchors that consist of
      collagen-based bodies, ceramic washers, and polyester sutures. Eighteen
      rabbits underwent bilateral implantations in the distal femoral condyles.
      Nine animals received glutaraldehyde-crosslinked fibrillar collagen bone
      anchors (FC) and 9 received glutaraldehyde-crosslinked fibrillar collagen
      bone anchors containing tricalcium phosphate (FC-TCP). Three animals per
```

group were sacrificed at postimplantation weeks 1, 6, and 12. One femur from each rabbit was evaluated histol., and the contralateral side underwent biomech. pull-out testing. Histol. evaluation of the implant site indicated that the FC and FC-TCP bone anchors were both biocompatible. The FC-TCP formulation degraded earlier than the FC formulation, and FC-TCP showed significant degradation at 6 wk; the FC and FC-TCP formulations both showed similar amts. of degradation at 12 wk. The degrading anchor bodies appeared to be osteoconductive as evidenced by new bone ingrowth into the degrading collagen matrixes without a fibrous interface. Collagen-based bone anchors have potential as bioresorbable orthopedic implants.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:490548 HCAPLUS
DOCUMENT NUMBER: 129:127205
TITLE: Methods and apparatuses for making swellable uniformly shaped devices from polymeric materials
INVENTOR(S): Yeung, Jeffrey E.; Schroeder, Jacqueline A.; **Brown, Melissa K. C.**; Shenoy, Vivek N.
PATENT ASSIGNEE(S): Cohesion Technologies, Inc., USA; Yeung, Jeffrey E.; Schroeder, Jacqueline A.; Brown, Melissa K. C.; Shenoy, Vivek N.
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9830252	A1	19980716	WO 1998-US530	19980108
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9860215	A1	19980803	AU 1998-60215	19980108
PRIORITY APPLN. INFO.:			US 1997-781012	19970109
			US 1997-833874	19970410
			WO 1998-US530	19980108

AB Disclosed herein are uniformly shaped swellable devices comprising polymeric materials, as well as apparatuses and processes for their manufacture In one embodiment, the present invention relates to load bearing implant devices for use in tissue repair. The implants consist of a resorbable, swellable implant body which is formed from a dehydrated cross-linked biocompatible polymer. As such, the implants are capable of swelling after insertion to become anchored in place. The implants function to enhance the structural integrity of the hard tissue into which they are placed, and thereby improve the load bearing capacity of such tissues. The implants are particularly well suited for use in attaching a second (hard or soft) tissue to the first (hard) tissue into which the implant is inserted. They may also be used as a site for attachment of a surgical

device such as a screw, rod or pin. An example is given for prepared of collagen-based bone suture anchor using glutaraldehyde crosslinking agent.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:189189 HCAPLUS
DOCUMENT NUMBER: 128:266165
TITLE: A comparison of the hemodynamic effects of propofol and isoflurane in pregnant ewes
AUTHOR(S): Gaynor, J. S.; Wertz, E. M.; **Alvis, M.**; Turner, A. S.
CORPORATE SOURCE: Department of Clinical Sciences, Colorado State University, Fort Collins, CO, 80523, USA
SOURCE: Journal of Veterinary Pharmacology and Therapeutics (1998), 21(1), 69-73
CODEN: JVPTD9; ISSN: 0140-7783
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to compare the effects of inhaled isoflurane and a constant infusion of propofol on maternal hemodynamics and uterine arterial and umbilical venous flows in pregnant ewes. Late term pregnant ewes (n = 5) were randomly assigned to receive either inhaled isoflurane or an i.v. infusion of propofol for 1 h, each on sep. occasions. Maternal systemic arterial, right atrial and pulmonary arterial blood pressures, cardiac index, systemic vascular resistance index, stroke volume index, heart rate, and uterine arterial and umbilical venous flows were determined over the 1 h period of each treatment. Data were analyzed using an univariate anal. of variance for repeated measures performed on the ranks of the data. Propofol anesthetized ewes had significantly higher heart rate ($P = 0.0040$), mean arterial pressure ($P = 0.0003$) and cardiac index ($P = 0.0475$) compared to isoflurane anesthetized ewes. There were no significant differences in uterine arterial flows, umbilical venous flows, or other measured variables. Continuous propofol infusions maintain maternal hemodynamics at significantly higher levels than does inhaled isoflurane, while uterine arterial and umbilical venous flows do not differ significantly.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:936054 HCAPLUS
DOCUMENT NUMBER: 123:330321
TITLE: Dose-response effects of estradiol implants on bone mineral density in ovariectomized ewes
AUTHOR(S): Turner, A. S.; Mallinckrodt, C. H.; **Alvis, M. R.**; Bryant, H. U.
CORPORATE SOURCE: Department Clinical Sciences, Colorado State University, Ft. Collins, CO, 80523, USA
SOURCE: Bone (New York) (1995), 17(4, Suppl., Proceedings of the International Conference on Animal Models in the Prevention and Treatment of Osteopenia, 1995), 421s-7s
CODEN: BONEDL; ISSN: 8756-3282
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a longitudinal in vivo study, the authors studied the effect of two

different doses of 17β-estradiol (E2) administered in the form of a s.c. implant, on bone mineral d. (BMD) of the lumbar vertebrae (L4, L5, L4-L6/L5-L7), the calcaneus (CAL) and the distal radius (DR) in ovariectomized (OVX) ewes. The BMD of various regions of the femur, tibia and humerus were studied at autopsy. Skeletally mature ewes were divided into four groups: sham operated, OVX, OVX plus one E2 implant (OVXE) and OVX plus two E2 implants (OVX2E). BMD of L4, L5, L4-L6/L5-L7, CAL and DR was determined at 0, 6 and 12 mo using dual-energy x-ray absorptiometry. In-vivo precision of BMD for the last three lumbar vertebrae ranged from 1.4-4.3%, and 1.5% and 3.5% for CAL and DR resp. In the in vivo study, there were no significant changes in the mean BMD in the sham group at any time point (each group served as its own control). In the OVX group, mean BMD was significantly lower at L5 and DR at 6 mo and significantly lower at L4 at 12 mo. In the OVXE group, the mean BMD was significantly higher at L5, CAL and DR at 12 mo. In the OVX2E group, BMD was significantly higher at CAL but significantly lower at L4 at 12 mo. None of the treatments produced significant changes of mean BMD of L4-L6/L5-L7 at any time point. Treatment influenced the rate of change in BMD for L4 and L5 (0.041 resp.) but not at other locations between 0 and 12 mo (repeated measures ANOVA). The sham and OVXE groups lost less bone than the OVX and the OVX2E groups (each group served as its own control). After 12 mo, ex-vivo measurement of BMD of the proximal and distal femur, proximal tibia and proximal humerus without soft tissues, showed no significant difference between the four treatment groups. The slight decrease in bone mass in the ewe following OVX was expected but the authors were surprised to see a decrease in BMD of similar magnitude in L4 but increases in BMD of L5, CAL and DR in those animals with two E2 implants with time. The authors suspect that a continuous supraphysiol. dose of E2 may have desensitized the bone by downregulating estrogen receptors. L4, L5 are critical sites where BMD can be measured to evaluate therapies if this model is used. The CAL and DR have not been as promising.

L10 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:936051 HCAPLUS
DOCUMENT NUMBER: 124:52740
TITLE: Changes in bone mineral density and bone-specific alkaline phosphatase in ovariectomized ewes
AUTHOR(S): Turner, A. S.; **Alvis, M.**; Myers, W.; Stevens, M. L.; Lundy, M. W.
CORPORATE SOURCE: Department Clinical Sciences, Colorado State University, Ft. Collins, CO, 80523, USA
SOURCE: Bone (New York) (1995), 17(4, Suppl., Proceedings of the International Conference on Animal Models in the Prevention and Treatment of Osteopenia, 1995), 395s-402s
CODEN: BONEDL; ISSN: 8756-3282
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An animal model of human osteoporosis which adequately meets many of the criteria needed to test new therapeutic agents is currently unavailable. The old ewe may serve this purpose, as changes in bone remodeling occur within 3 mo, and a difference in bone mass has been indicated 6 mo after ovariectomy. In the current study, the authors have measured longitudinal changes in bone mass and bone-specific alkaline phosphatase (BSAP) for six months in 7-9 yr old ovariectomized (OVX) ewes. Thirty ewes were divided into three groups: sham-treated, OVX and OVX with estrogen implants (OVXE). Bone mineral d. (BMD) was determined at 0, 3 and 6 mo in the vertebrae

(L4-L6/L5-L7), calcaneus (CAL) and distal radius (DR) using dual-energy x-ray absorptiometry (DEXA). Bone-Specific Alkaline Phosphatase (Tandem ®-R OstaseTM; Hybritech) was determined at monthly intervals. Body weight did not significantly change in any group during treatment compared to sham, although a trend of increasing body weight at 3 and 6 mo was apparent in both OVX groups. LH increased in all OVX ewes as a function of time as expected, demonstrating successful ovariectomies. Uterine weight was significantly increased in the OVXE animals compared to Sham and OVX groups. BMD did not change significantly during the 6-mo treatment period in the CAL or DR. BMD in the vertebrae (L4-L6/L5-L7) was significantly lower in the OVX group compared to sham. Estrogen significantly increased BMD (L4-L6/L5-L7) compared to both the sham and OVX groups. Estrogen treatment did not change BSAP at any time point compared to sham, however OVX significantly increased BSAP at both 3 and 6 mo compared to sham and estrogen groups. The results confirm earlier studies indicating an increase in bone remodeling rates by 3 mo in OVX ewes and demonstrated a change in bone mass between the sham and OVX groups six months after OVX. The mechanisms leading to the increase in BMD following estrogen treatment are not clear. This study in old ewes suggests that this may be a useful model for long-term studies investigating estrogen-deficiency induced bone loss in a remodeling species.

=> b home
FILE 'HOME' ENTERED AT 16:34:30 ON 16 SEP 2004

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=> b reg
FILE 'REGISTRY' ENTERED AT 16:32:25 ON 16 SEP 2004
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STRUCTURE FILE UPDATES:   15 SEP 2004  HIGHEST RN 745743-57-1
DICTIONARY FILE UPDATES:  15 SEP 2004  HIGHEST RN 745743-57-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que l55
L11           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  COLLAGENS/CN
L46           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "ATELOCOLLAGEN SS"/CN
L55           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 OR L46


=> d ide

L55  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   9007-34-5  REGISTRY *
* Use of this CAS Registry Number alone as a search term in other STN files may
  result in incomplete search results.  For additional information, enter HELP
  RN* at an online arrow prompt (=>).
CN   Collagens  (CA INDEX NAME)
OTHER NAMES:
CN   Alfomarine CL
CN   Atelocollagen SS
CN   Avitene
CN   Biofine P 116
CN   Biofleece
CN   BioMend
CN   Cellmatrix Type I-A
CN   Collagen Powder FGH
CN   Collagenon
CN   Collapton S
CN   CX 285
CN   Dermalogen
CN   Ergona P 100X
CN   Ergona P 160X
CN   EZ 3
CN   HCP-M 15
CN   Helistat
CN   Hemostagene
CN   Kokencellgen I-PC
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CN MC 1243Z
CN MC 1245A
CN MCP 1
CN MCP 1 (protein)
CN Neptigen N
CN Neptigen Naturaltype
CN Nippi Peptide PBF
CN Nippi Peptide PRA
CN Novacol
CN Orprotein RO
CN Pancogen Marin
CN Pangen
CN PK 100
CN PK 100 (protein)
CN Rakuset KG
CN Serva 17440
CN Tachotop
CN Toriazet
CN Toriazet CX 260-1
CN Toriazet CX 260-3
CN Toriazet CX 285-1
CN Toriazet LQ
CN Toriazet LX 260-1
CN ZA 552
CN Zyderm
CN Zyderm II
DEF A fibrous protein comprising one third of the total protein in mammalian organisms. It is a polypeptide containing three peptide chains and rich in proline and hydroxyproline.
DR 55963-88-7, 93685-58-6, 92113-30-9, 157970-72-4
MF Unspecified
CI PMS, MAN, CTS
PCT Manual registration
LC STN Files: ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PHAR, TOXCENTER
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FILE 'HOME' ENTERED AT 16:32:46 ON 16 SEP 2004

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=> b hcaplus
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FILE COVERS 1907 - 16 Sep 2004  VOL 141 ISS 12
FILE LAST UPDATED: 15 Sep 2004  (20040915/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que l53
L11            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  COLLAGENS/CN
L13         8392 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
                 SUSTAINED-RELEASE"+NT,OLD/CT
L14        12428 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((SUSTAIN?/OBI OR EXTEN?/OBI)(
                 2A)(RELEAS?/OBI OR ACTION?/OBI)) OR L13
L46            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "ATELOCOLLAGEN SS"/CN
L51          407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "COLLAGENS (L) ATELOCOLLAGENS"
                 +OLD/CT
L52           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L51 OR L11 OR L46 OR
                 ATELOCOLLAG?/OBI OR ATELOPEPT?/OBI(A)COLLAG?/OBI) AND L14
L53           12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L52 AND P/DT


=> b medl
FILE 'MEDLINE' ENTERED AT 16:26:46 ON 16 SEP 2004

 FILE LAST UPDATED: 15 SEP 2004 (20040915/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l21
L20           95 SEA FILE=MEDLINE ABB=ON  PLU=ON  ATELOCOLLAGEN/CN
L21            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  (SUSTAIN? OR EXTEN?) AND L20
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=> b embase
FILE 'EMBASE' ENTERED AT 16:26:56 ON 16 SEP 2004
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 FILE COVERS 1974 TO 9 Sep 2004 (20040909/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> d que l30
L24          116 SEA FILE=EMBASE ABB=ON  PLU=ON  ATELOCOLLAGEN/CT
L26          690 SEA FILE=EMBASE ABB=ON  PLU=ON  "SUSTAINED DRUG RELEASE"/CT
L27          617 SEA FILE=EMBASE ABB=ON  PLU=ON  "SUSTAINED RELEASE FORMULATION"
                 /CT
L28        12177 SEA FILE=EMBASE ABB=ON  PLU=ON  "SUSTAINED RELEASE PREPARATION"
                 /CT
L29        13402 SEA FILE=EMBASE ABB=ON  PLU=ON  (L26 OR L27 OR L28)
L30            4 SEA FILE=EMBASE ABB=ON  PLU=ON  L24 AND L29


=> b biosis
FILE 'BIOSIS' ENTERED AT 16:27:12 ON 16 SEP 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 15 September 2004 (20040915/ED)

FILE RELOADED: 19 October 2003.

=> d que l32
L31           14 SEA FILE=BIOSIS ABB=ON  PLU=ON  ATELOCOLLAGEN? AND (SUSTAIN?
                 OR EXTEN?)
L32           11 SEA FILE=BIOSIS ABB=ON  PLU=ON  L31 AND PY<=2002


=> b wpix
FILE 'WPIX' ENTERED AT 16:27:24 ON 16 SEP 2004
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FILE LAST UPDATED:          15 SEP 2004      <20040915/UP>
MOST RECENT DERWENT UPDATE:     200459        <200459/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
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    HIT STRUCTURES WITHIN THE BIBLIOGRAPHIC DOCUMENT  <<<

=> d que l42
L41           74 SEA FILE=WPIX ABB=ON  PLU=ON  ATELOCOLLAG?/BIX
L42           10 SEA FILE=WPIX ABB=ON  PLU=ON  B12-M10?/MC AND L41


=> dup rem l32 l21 l30 l53 l42
FILE 'BIOSIS' ENTERED AT 16:28:07 ON 16 SEP 2004
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FILE 'WPIX' ENTERED AT 16:28:07 ON 16 SEP 2004
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PROCESSING COMPLETED FOR L32
PROCESSING COMPLETED FOR L21
PROCESSING COMPLETED FOR L30
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L42
L54           36 DUP REM L32 L21 L30 L53 L42 (6 DUPLICATES REMOVED)

=> d ibib abs hitind l54 1-36

L54  ANSWER 1 OF 36  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:651038  HCAPLUS
DOCUMENT NUMBER:          141:179705
TITLE:                    Dental materials containing self-regenerating
                          substances
INVENTOR(S):              Nakahara, Takashi
PATENT ASSIGNEE(S):       Tapic International Co., Ltd., Japan
SOURCE:                   Jpn. Kokai Tokkyo Koho, 9 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
     JP 2004222993         A2    20040812    JP 2003-14827          20030123
PRIORITY APPLN. INFO.:                       JP 2003-14827          20030123
AB   Title materials comprise regenerated atelocollagen containing ≥1
     self-regenerating substances.  Thus, bFGF-impregnated gelatin fine
     particles sandwiched between regenerated atelocollagen sheets were
     implanted in a cavity created by tooth extraction to regenerate bone, capillary
     blood vessels, and cells.
```

IC ICM A61L027-00
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 1, 2
ST bFGF **atelocollagen** dental self regeneration; basic fibroblast growth factor dental self regeneration
IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**atelocollagens**; regenerated **atelocollagen** containing self-regenerating substance-containing gelatin for treatment of periodontal tissue)
IT Cell differentiation
(factors for; regenerated **atelocollagen** containing self-regenerating substance-containing gelatin for treatment of periodontal tissue)
IT Dental materials and appliances
(implants; regenerated **atelocollagen** containing self-regenerating substance-containing gelatin for treatment of periodontal tissue)
IT Antibiotics
Fungicides
Nutrients
Periodontium
Regeneration, animal
Wound healing promoters
(regenerated **atelocollagen** containing self-regenerating substance-containing gelatin for treatment of periodontal tissue)
IT Gelatins, biological studies
Growth factors, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regenerated **atelocollagen** containing self-regenerating substance-containing gelatin for treatment of periodontal tissue)
IT **Drug delivery systems**
(**sustained-release**; regenerated **atelocollagen** containing self-regenerating substance-containing gelatin for treatment of periodontal tissue)
IT 106096-93-9, Basic fibroblast growth factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regenerated **atelocollagen** containing self-regenerating substance-containing gelatin for treatment of periodontal tissue)

L54 ANSWER 2 OF 36 EMBASE
on STN
ACCESSION NUMBER: 2004168890 EMBASE
TITLE: Controlled release of rhBMP-2 from collagen minipellet and the relationship between release profile and ectopic bone formation.
AUTHOR: Maeda H.; Sano A.; Fujioka K.
CORPORATE SOURCE: H. Maeda, Formulation Research Laboratories, Sumitomo Pharmaceuticals Co. Ltd., 3-45 Kurakakiuchi 1-Chome, Ibaraki-shi, Osaka 567-0878, Japan.
maedah@sumitomopharm.co.jp
SOURCE: International Journal of Pharmaceutics, (4 May 2004) 275/1-2 (109-122).
Refs: 31
ISSN: 0378-5173 CODEN: IJPHDE
PUBLISHER IDENT.: S 0378-5173(04)00083-3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index

039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The purpose of this study was to examine the effects of various additives on the profiles of rhBMP-2 release from minipellet, which is a sustained release formulation for protein drugs using collagen as a carrier, and to examine the influence of varying release profiles on ectopic bone formation. When the amount of rhBMP-2 remaining in the preparation after subcutaneous implantation to mice was examined, it was found that the addition of sucrose, glucose, PEG4000, alanine (Ala) or acacia in a concentration of 20% (w/w) to the minipellet with 5% (w/w) of rhBMP-2 did not accelerate the drug release in a noticeable manner, while the addition of sodium chondroitin sulfate, glutamic acid (Glu) or citric acid accelerated the release of rhBMP-2 markedly. When two types of minipellets (a fast release type added with 20% Glu and 20% Ala and a slow release type without additives) containing varying amounts of rhBMP-2 were implanted subcutaneously to mice, the soft X-ray observation, histological examination and measurement of calcium formation 3 weeks after implantation revealed extensive ectopic bone formation in mice implanted with the fast release type preparation. Ectopic bone formation was dose-dependent. The result of this study exhibited that the effects of controlled release formulation of rhBMP-2 on bone formation vary depending on their release profiles, and suggested that combination of initial burst and sustained release was effective for bone formation. It was also shown that minipellet is useful as a controlled release formulation which can release rhBMP-2 to areas around the implanted site with various release profiles.
CT Medical Descriptors:
*pellet extrusion
*ectopic tissue
*ossification
***sustained drug release**
implant
X ray analysis
histology
drug dose regimen
dose response
slow drug release
nonhuman
male
mouse
controlled study
animal tissue
article
priority journal
Drug Descriptors:
*recombinant bone morphogenetic protein 2: DO, drug dose
*recombinant bone morphogenetic protein 2: PR, pharmaceutics
*recombinant bone morphogenetic protein 2: PD, pharmacology
drug carrier: PR, pharmaceutics
atelocollagen: PR, pharmaceutics
sucrose: PR, pharmaceutics
glucose: PR, pharmaceutics
macrogol 4000: PR, pharmaceutics
alanine: PR, pharmaceutics
chondroitin sulfate: PR, pharmaceutics
glutamic acid: PR, pharmaceutics
citric acid: PR, pharmaceutics
calcium
RN (sucrose) 122880-25-5, 57-50-1; (glucose) 50-99-7, 84778-64-3; (macrogol

4000) 88747-22-2; (alanine) 56-41-7, 6898-94-8; (chondroitin sulfate) 9007-28-7, 9082-07-9; (glutamic acid) 11070-68-1, 138-15-8, 56-86-0, 6899-05-4; (citric acid) 126-44-3, 5949-29-1, 77-92-9, 8002-14-0; (calcium) 7440-70-2

CO Koken (Japan); Wyeth (United States)

L54 ANSWER 3 OF 36 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-596952 [56] WPIX
DOC. NO. CPI: C2003-161669
TITLE: New controlled or sustained release gene preparations for the subcutaneous, intramuscular or intraperitoneal delivery of a gene for uptake by a cell of a subject, useful in medicine, especially gene therapy.
DERWENT CLASS: B04 B07 D16
INVENTOR(S): ITOH, H; MIYATA, T; OCHIYA, T; TERADA, M
PATENT ASSIGNEE(S): (ITOH-I) ITOH H; (MIYA-I) MIYATA T; (OCHI-I) OCHIYA T; (TERA-I) TERADA M
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003082161	A1	20030501	(200356)*		11

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003082161	A1 CIP of	US 1998-981552	19980204
		US 2002-261618	20021002

PRIORITY APPLN. INFO: US 2002-261618 20021002; US 1998-981552 19980204
AN 2003-596952 [56] WPIX
AB US2003082161 A UPAB: 20030903
NOVELTY - New controlled or sustained release gene preparations, which:
(a) comprise **atelocollagen** (0.01-25 w/w % of the preparation), an additive, and an intended gene or vector comprising the gene; or
(b) is obtained by drying a gel, comprises 0.2-30 (preferably 10-30) w/w % of **atelocollagen**, an additive, and an intended gene or vector comprising the gene.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for methods for delivering a gene for uptake by a cell of a subject by administering the controlled or sustained release gene preparations. The preparation is administered subcutaneously, intramuscularly or intraperitoneally.
ACTIVITY - None Given.
MECHANISM OF ACTION - Gene Therapy.
USE - The gene preparations or methods are useful in medicine, especially gene therapy. The gene preparations are particularly useful for delivering a gene for uptake by a cell of a subject, providing a high frequency of transformation, and regulating gene expression.
Dwg.0/6

L54 ANSWER 4 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2002415994 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12054709
TITLE: Regeneration of defects in the articular cartilage in

rabbit temporomandibular joints by bone morphogenetic protein-2.

AUTHOR: Suzuki T; Bessho K; Fujimura K; Okubo Y; Segami N; Iizuka T
CORPORATE SOURCE: Department of Oral and Maxillofacial Surgery, Kanazawa Medical University, Ishikawa, Japan.

SOURCE: British journal of oral & maxillofacial surgery, (2002 Jun) 40 (3) 201-6.
Journal code: 8405235. ISSN: 0266-4356.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020813
Last Updated on STN: 20021212
Entered Medline: 20021108

AB The purpose of this study was to investigate the therapeutic use of recombinant human bone morphogenetic protein-2 (rhBMP-2) in internally deranged temporomandibular joints (TMJ). Defects (2 mm in diameter) were created in the surface of the condylar head. Lyophilized rhBMP-2 with collagen as the carrier was implanted in the defects in different doses: rhBMP-2 15 microg (n = 5); rhBMP-2 3 microg (n = 5); rhBMP-2 0.6 microg (n = 5). In the two control groups, the defects were either filled with collagen alone (n = 5) or left untreated (n = 5). Three weeks postoperatively the sites of defects were examined under light microscopy. In the 15 micromg and the 3 microg groups, new cartilage had filled the defects; endochondral ossification was also found deep within the defect. In the 0.6 microg group, fibrous tissue was proliferating in most areas of the defect, although cartilage was also found in some parts. In the two control groups, there was either soft tissue repair only or no evidence of tissue repair. These findings suggest that BMP-2 could stimulate the repair of defects in the articular cartilage of the mandibular condyle head during the 3 weeks postoperatively. To observe the progress of endochondral ossification in more detail, it may be necessary to **extend** the experiment for a longer period of time. However, this study supports the contention that BMP-2 may be useful in the regeneration of cartilage in TMJ disease.

CT Check Tags: Human; Support, Non-U.S. Gov't
Animals
Bone Morphogenetic Proteins: AD, administration & dosage
*Bone Morphogenetic Proteins: TU, therapeutic use
*Cartilage Diseases: DT, drug therapy
Cartilage Diseases: PA, pathology
*Cartilage, Articular: DE, drug effects
Cartilage, Articular: PA, pathology
Chondrocytes: DE, drug effects
Chondrocytes: PA, pathology
Chondrogenesis: DE, drug effects
Collagen
Connective Tissue: DE, drug effects
Connective Tissue: PA, pathology
Drug Carriers
Drug Implants
Mandibular Condyle: DE, drug effects
Mandibular Condyle: PA, pathology
Osteogenesis: DE, drug effects
Rabbits
Recombinant Proteins
Regeneration: DE, drug effects

Temporomandibular Joint Disk: DE, drug effects
Temporomandibular Joint Disk: PA, pathology
*Temporomandibular Joint Disorders: DT, drug therapy
Temporomandibular Joint Disorders: PA, pathology
Time Factors
Transforming Growth Factor beta: AD, administration & dosage
*Transforming Growth Factor beta: TU, therapeutic use
Wound Healing: DE, drug effects
RN 9007-34-5 (Collagen)
CN 0 (Bone Morphogenetic Proteins); 0 (Drug Carriers); 0 (Drug Implants); 0 (Recombinant Proteins); 0 (Transforming Growth Factor beta); **0 (atelocollagen)**; 0 (bone morphogenetic protein 2)

L54 ANSWER 5 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:392864 BIOSIS
DOCUMENT NUMBER: PREV200100392864
TITLE: Preparation of collagen modified hyaluronan microparticles as antibiotics carrier.
AUTHOR(S): Lee, Jong-Eun; Park, Jong-Chul; Kim, Joong-Gon; Suh, Hwal [Reprint author]
CORPORATE SOURCE: Department of Medical Engineering, Yonsei University College of Medicine, Seoul, 120-752, South Korea hwal@yumc.yonsei.ac.kr
SOURCE: Yonsei Medical Journal, (June, 2001) Vol. 42, No. 3, pp. 291-298. print.
CODEN: YOMJA9. ISSN: 0513-5796.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2001
Last Updated on STN: 22 Feb 2002

AB Hyaluronan (HA), a natural glycoaminoglycan featuring an extracellular matrix, has been suggested as an effective biocompatible material. In this study, the effectiveness of HA microparticles as a carrier system for antibiotics was evaluated, and their physicochemical characteristics were determined. Microparticles were fabricated by the gelation of sulfadiazine (SD) loaded HA solution with calcium chloride through either a granulation (GR-microparticles) or encapsulation (EN-microparticles) process, and **atelocollagen** was incorporated into the microparticles as an additive in order to improve their physical properties. The characteristics of the microparticles were examined by scanning electron microscopy (SEM), differential scanning calorimetry (DSC), and swelling test. In vitro release experiments were performed for 7 days and the released amount of SD was determined using high-performance liquid chromatography (HPLC). Microscopic observations revealed that the collagen incorporated HA particles had a more compact surface than the HA particles. DSC analysis determined a loss of SD crystallinity in the particles. Calcium chloride retarded the swelling of particles, whereas the loaded drug contents did not affect this property. Both GR-and EN-microparticles **sustained** SD release with initial bursting effect. SD release from EN-microparticles was faster than from GR-microparticles. In addition, the release rate was dependent on the SD content in the microparticles. These results suggest that collagen modified HA microparticles have a potential as a release rate controlling material for crystalline drugs such as SD.
CC Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Biochemistry studies - Minerals 10069
Pathology - Therapy 12512

Pharmacology - General 22002
Pharmacology - Drug metabolism and metabolic stimulators 22003
IT Major Concepts
Chemistry; Methods and Techniques; Pharmaceuticals (Pharmacology)
IT Chemicals & Biochemicals
calcium chloride; collagen; hyaluronan; sulfadiazine: pharmacokinetics, **sustained** release
IT Methods & Equipment
collagen modified hyaluronan microparticles: antibiotic carrier, drug delivery method, preparation; differential scanning calorimetry: analytical method; release test: drug evaluation method; scanning electron microscopy: analytical method, microscopy method
IT Miscellaneous Descriptors
encapsulation; granulation; pharmaceutical chemistry
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 10043-52-4 (calcium chloride)
9004-61-9 (hyaluronan)
68-35-9 (sulfadiazine)

L54 ANSWER 6 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:525044 BIOSIS
DOCUMENT NUMBER: PREV200000525044
TITLE: Studies on poly(propylene fumarate-co-ethylene glycol) based bone cement.
AUTHOR(S): Jayabalan, Muthu [Reprint author]; Thomas, Vinoy; Sreelatha, P. K.
CORPORATE SOURCE: Polymer Division, Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram-12, KER, India
SOURCE: Bio-Medical Materials and Engineering, (2000) Vol. 10, No. 2, pp. 57-71. print.
CODEN: BMENEO. ISSN: 0959-2989.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Dec 2000
Last Updated on STN: 11 Jan 2002
AB Poly(propylene fumarate-co-ethylene glycol) random (PPF-1) and block (PPF-2) copolymer oligomers were prepared. Comparing the setting characteristics of PPF-1 and PPF-2 with comonomer n-vinyl pyrrolidone (n-VP) and swelling characteristics of cured PPF-1 and PPF-2, lower setting temperature and setting time was observed with the former leading to higher swelling coefficient and lower cross link density in the cured PPF-1. Due to the high swelling coefficient and low setting exothermic temperature associated with PPF-1, the bone cement was prepared from PPF-1, n-VP and hydroxyapatite (HAP). The in vitro degradation studies reveal lesser weight loss and deformation of PPF-1/n-VP/HAP based cured resin in Ringer's solution and phosphate buffered saline in comparison with that of PPF-1/n-VP cured resin. Though the bone cement composite has adequate mechanical properties with HAP, the compressive strength and modulus of the composite aged in Ringer's solution and PBS reduced appreciably which is due to **extensive** hydration and plasticization by the PEG unit. However, the bone-binding and bond

strength of the bone cement determined as the load for separation of bones was found to be similar to that of fast setting calcium phosphate - **atelocollagen** (5%) bone cement. The bone cement PPF-1/n-VP/HAP could be used as scaffold for correcting the bone defects.

CC Biophysics - Bioengineering 10511
Bones, joints, fasciae, connective and adipose tissue - Physiology and biochemistry 18004

IT Major Concepts
Biomaterials; Skeletal System (Movement and Support)

IT Parts, Structures, & Systems of Organisms
bones: skeletal system, defect correction

IT Chemicals & Biochemicals
phosphate; poly(propylene fumarate-co-ethylene glycol)-based bone cements: analysis, applications, setting characteristics, swelling characteristics

ORGN Classifier
Bovidae 85715
Super Taxa
Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
bovine
Taxa Notes
Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

RN 14265-44-2 (phosphate)

L54 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:763907 HCAPLUS
DOCUMENT NUMBER: 132:6372
TITLE: Stable therapeutic gene preparations
INVENTOR(S): Terada, Masaaki; Ochiya, Takahiro; Sano, Akihiko; Hisada, Akihiko; Nagahara, Shunji
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan; Koken Co., Ltd.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961063	A1	19991202	WO 1999-JP2595	19990519
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2329129	AA	19991202	CA 1999-2329129	19990519
AU 9938488	A1	19991213	AU 1999-38488	19990519
AU 755126	B2	20021205		
EP 1078639	A1	20010228	EP 1999-921163	19990519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
NZ 508785	A	20031031	NZ 1999-508785	19990519
PRIORITY APPLN. INFO.:			JP 1998-141426 A	19980522

WO 1999-JP2595 W 19990519

AB Disclosed are formulations for gene therapy capable of sustaining high stability during the production process and storage. These formulations contain saccharides, non-hydrophobic amino acids, and/or organic acids having ≥2 carboxyl groups (excluding amino acids), or collagen or gelatin and at least one amino acid. A sustained-release stick preparation was prepared from 100 μg/mL plasmid vector pCAHST-1 (encoding FGF-4) solution 80 mL, 0.86 % atelocollagen solution 29.1, water 60 g, and 11 mg/mL glucose solution 10 mL.

IC ICM A61K048-00

CC 63-6 (Pharmaceuticals)

ST gene therapy stabilizer saccharide amino acid; **sustained release** plasmid vector **atelocollagen** glucose

IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**atelocollagens**; stabilized gene formulations containing amino acids or carboxylates or saccharides)

IT **Drug delivery systems**
(implants, **sustained-release**; stabilized gene formulations containing amino acids or carboxylates or saccharides)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:468186 HCAPLUS

DOCUMENT NUMBER: 131:106873

TITLE: Shape-forming collagen gels for ophthalmological use

INVENTOR(S): Nemoto, Kazuki; Ito, Hiroshi; Nagai, Hiroshi

PATENT ASSIGNEE(S): Koken Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF

DOCUMENT TYPE: **Patent**

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11197234	A2	19990727	JP 1998-2770	19980109

PRIORITY APPLN. INFO.: JP 1998-2770 19980109

AB Shape-forming collagen gels for ophthalmol. use [e.g. for preparing contact lenses and eye sustained-release pharmaceuticals] are prepared from soluble collagens and crosslinking agents. The prepns. are transparent and temperature denaturation-resistant.

IC ICM A61L027-00
ICS G02B007-04; G02C007-04

CC 63-7 (Pharmaceuticals)

ST collagen gel ophthalmol; contact lens collagen gel; eye **sustained release** pharmaceutical collagen gel

IT **Collagens, biological studies**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**atelocollagens**; shape-forming collagen gels for ophthalmol. use)

IT **Drug delivery systems**
(gels, **sustained-release**; shape-forming collagen gels for ophthalmol. use)

IT **Drug delivery systems**

(**sustained-release**; shape-forming collagen gels for ophthalmol. use)

L54 ANSWER 9 OF 36 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999218343 EMBASE
TITLE: New delivery system for plasmid DNA in vivo using atelocollagen as a carrier material: The Minipellet.
AUTHOR: Ochiya T.; Takahama Y.; Nagahara S.; Sumita Y.; Hisada A.; Itoh H.; Nagai Y.; Terada M.
CORPORATE SOURCE: M. Terada, Natl. Can. Center Research Institute, 1-1, Tsukiji, Chuo-ku, Tokyo 104, Japan
SOURCE: Nature Medicine, (1999) 5/6 (707-710).
Refs: 30
ISSN: 1078-8956 CODEN: NAMEFI
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
CT Medical Descriptors:
*gene transfer
*drug delivery system
sustained release preparation
kinetics
vaccination
nonhuman
mouse
controlled study
adolescent
intramuscular drug administration
review
priority journal
Drug Descriptors:
***atelocollagen: PR, pharmaceutics**
*plasmid DNA
*fibroblast growth factor 4: EC, endogenous compound

L54 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:277491 HCAPLUS
DOCUMENT NUMBER: 128:326532
TITLE: **Sustained-release** formulation containing collagen and glycosaminoglycan
INVENTOR(S): Koseki, Norimasa; Sano, Akihiko
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 838219	A1	19980429	EP 1997-117479	19971009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CA 2217134	AA	19980409	CA 1997-2217134	19970930
AU 9739907	A1	19980423	AU 1997-39907	19971006

AU 727049 B2 20001130
JP 10167987 A2 19980623 JP 1997-293472 19971009
US 5922356 A 19990713 US 1997-947463 19971009
PRIORITY APPLN. INFO.: JP 1996-268801 A 19961009

AB The present invention relates to a sustained-release formulation used for the treatment or prevention of diseases, which contains a therapeutically effective substance as an active ingredient, collagen as a drug carrier, and glycosaminoglycan as an additive. The formulation allows controlled release of the therapeutically effective substance. To a 2 % (weight/volume) atelocollagen solution (14.9 g), a chondroitin-6-sulfate solution (10 mg/mL, 0.3 mL) was added and an α-interferon solution (100 MIU/mL, 4.4 mL) was admixed thereto. The mixture was lyophilized and an appropriate quantity of distilled was added to give a mixture, which was kneaded, extruded, and then dried to give a cylindrical preparation

IC ICM A61K009-20
CC 63-6 (Pharmaceuticals)
ST **sustained release** glycosaminoglycan collagen drug carrier; interferon **atelocollagen** chondroitin sulfate **sustained release**
IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**atelocollagens; sustained-release** formulation containing collagens and glycosaminoglycans)
IT Gene
Glycoproteins, general, biological studies
Peptides, biological studies
Polysaccharides, biological studies
Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. active; **sustained-release** formulation containing collagens and glycosaminoglycans)
IT Collagens, biological studies
Glycosaminoglycans, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**sustained-release** formulation containing collagens and glycosaminoglycans)
IT **Drug delivery systems**
(**sustained-release; sustained-release** formulation containing collagens and glycosaminoglycans)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α; **sustained-release** formulation containing collagens and glycosaminoglycans)
IT 9001-63-2, Lysozyme 9004-61-9, Hyaluronic acid 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 24967-94-0, Dermatan sulfate 25322-46-7, Chondroitin-6-sulfate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**sustained-release** formulation containing collagens and glycosaminoglycans)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 11 OF 36 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-433777 [37] WPIX
DOC. NO. CPI: C1998-131154
TITLE: Sustained release composition - comprises soluble collagen and/or its derivatives support and medical compound.
DERWENT CLASS: A96 B07

PATENT ASSIGNEE(S): (KOKE) KOKEN KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 10182499	A	19980707	(199837)*		4
JP 3240593	B2	20011217	(200203)		4

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 10182499	A Div ex	JP 1989-230421	19890907
		JP 1998-48559	19890907
JP 3240593	B2 Div ex	JP 1989-230421	19890907
		JP 1998-48559	19890907

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 3240593	B2 Previous Publ.	JP 10182499

PRIORITY APPLN. INFO: JP 1989-230421 19890907; JP 1998-48559 19890907
AN 1998-433777 [37] WPIX
AB JP 10182499 A UPAB: 19980916
Substained release composition comprises a soluble collagen and/or its derivatives support and at least 1 medical compound. The particle diameter of the composition is 1-10 mu m.

The collagen preferably comprises **atelocollagen**, acid-soluble collagen, alkali-extracted collagen or collagen derivatives such as acylcollagen, methyl collagen or ethyl collagen.

ADVANTAGE - The composition can be used at any body part and is stably preserved.

Dwg.0/2

L54 ANSWER 12 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:39678 BIOSIS
DOCUMENT NUMBER: PREV199900039678
TITLE: Local application of basic fibroblast growth factor minipellet induces the healing of segmental bony defects in rabbits.
AUTHOR(S): Inui, K. [Reprint author]; Maeda, M.; Sano, A.; Fujioka, K.; Yutani, Y.; Sakawa, A.; Yamano, Y.; Kato, Y.; Koike, T.
CORPORATE SOURCE: Dep. Orthopaedic Surgery, Osaka City Univ. Med. Sci., 1-5-7 Asahimachi, Abeno-ku, Osaka 545-8585, Japan
SOURCE: Calcified Tissue International, (Dec., 1998) Vol. 63, No. 6, pp. 490-495. print.
CODEN: CTINDZ. ISSN: 0171-967X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Feb 1999
Last Updated on STN: 3 Feb 1999
AB Fibroblast growth factor (FGF) has been reported to increase the volume of callus in a fracture model of rats. There are, however, no reports of successful repair of segmental bony defects by application of an FGF solution. In this study, the effects of basic FGF on the repair of

segmental bony defects in the rabbit femur were examined. Minipellet, a new drug delivery system using **atelocollagen**, was employed to ensure effective delivery of FGF. Segmental bony defects (10 mm in length) were created in the right femurs of 19 rabbits. In pilot studies, no defects of this size healed spontaneously within 6 weeks. Bones were stabilized with miniexternal fixators. Minipellets containing basic FGF were implanted between fragments so as to bridge the two fragments. The healing processes were monitored radiographically and studied histologically. In rabbits in which FGF was added to the defect site at doses of 1.4 mug or higher, approximately 90% of the defects were filled with new bone and cartilage within 6 weeks after minipellet implantation. In rabbits receiving placebo minipellets, however, approximately 15% of the defects were filled by callus within 6 weeks. Furthermore, this callus did not change into defects had no effect on the repair of segmental bony defects. These findings suggest that FGF plays a role in the production of adequate volumes of callus particularly in the initial stages of fracture healing and that **sustained** local release enables FGF to be effective at a low dose. In summary, large segmental bony defects healed after insertion of low-dose FGF minipellets. An adequate dose of FGF and an appropriate delivery system are required for successful healing of large bony defects. These findings imply the potential value of FGF minipellets in clinical practice.

CC Pharmacology - General 22002
Biochemistry studies - General 10060
Pathology - Therapy 12512
Bones, joints, fasciae, connective and adipose tissue - General and methods 18001

IT Major Concepts
Pharmacology; Skeletal System (Movement and Support)

IT Parts, Structures, & Systems of Organisms
femur: skeletal system

IT Diseases
fracture: bone disease, injury
Fractures (MeSH)

IT Diseases
segmental bony defects: bone disease

IT Chemicals & Biochemicals
basic fibroblast growth factor: metabolic-drug

IT Miscellaneous Descriptors
wound healing

ORGN Classifier
Leporidae 86040
Super Taxa
Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rabbit
Taxa Notes
Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

RN 106096-93-9 (basic fibroblast growth factor)

L54 ANSWER 13 OF 36 EMBASE
on STN

ACCESSION NUMBER: 1998140289 EMBASE
TITLE: Protein release from collagen matrices.
AUTHOR: Fujioka K.; Maeda M.; Hojo T.; Sano A.
CORPORATE SOURCE: K. Fujioka, Manufacturing Technol. Res. Lab., Sumitomo Pharmaceuticals Co. Ltd., 3-45 Kurakakiuchi I-chome, Ibaraki-shi, Osaka 567, Japan
SOURCE: Advanced Drug Delivery Reviews, (4 May 1998) 31/3

(247-266).
Refs: 63
ISSN: 0169-409X CODEN: ADDREP
PUBLISHER IDENT.: S 0169-409X(97)00119-1
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The effective delivery of protein drugs is an important research subject in the field of pharmacology, and to prolong the effect of protein drugs, many studies are being conducted to control the release of proteins from various carrier materials. Collagen is one of the most useful candidates for this purpose, and many studies have been reported; pharmaceutical formulations containing collagen in gel, film and sponge form are used to incorporate low-molecular-weight compounds such as antibiotics and carcinostatics, and the release of these compounds is controlled by the concentration of the gel as well as the shape and degree of crosslinking of the matrix. However, it is still difficult to retain protein drugs in the collagen. In this article, we report on the controlled release of protein drugs using collagen which exhibits good biocompatibility as a carrier, focusing on a new drug delivery system, the Minipellet, which we have developed.

CT Medical Descriptors:
*controlled drug release
*drug delivery system
*drug pellet
gel
film
sponge
cross linking
biocompatibility
biodegradation
sustained release preparation
hepatitis c: DT, drug therapy
bone defect
human
nonhuman
clinical trial
phase 3 clinical trial
animal experiment
animal model
intracerebral drug administration
subcutaneous drug administration
intramuscular drug administration
article
priority journal
Drug Descriptors:
*collagen
*drug carrier
*interferon: CT, clinical trial
*interferon: DT, drug therapy
*interferon: PR, pharmaceutics
*interleukin 2: PR, pharmaceutics
*nerve growth factor: PR, pharmaceutics
*basic fibroblast growth factor: PR, pharmaceutics
biomaterial
albumin
gelatin

atelocollagen
antibiotic agent: PR, pharmaceutics
antineoplastic agent: PR, pharmaceutics
RN (collagen) 9007-34-5; (interleukin 2) 85898-30-2; (nerve growth factor) 9061-61-4; (basic fibroblast growth factor) 106096-93-9; (gelatin) 9000-70-8

L54 ANSWER 14 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1998:72050 BIOSIS
DOCUMENT NUMBER: PREV199800072050
TITLE: Bone morphogenetic protein induced repair of compartmentalized segmental diaphyseal defects.
AUTHOR(S): Teixeira, J. O. C.; Urist, M. R. [Reprint author]
CORPORATE SOURCE: UCLA Bone Res. Lab., Rehabilitation Cent., Room A3-34, 1000 Veteran Ave., Los Angeles, CA 90024, USA
SOURCE: Archives of Orthopaedic and Trauma Surgery, (Jan., 1998) Vol. 117, No. 1-2, pp. 27-34. print.
ISSN: 0936-8051.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 1998
Last Updated on STN: 20 Mar 1998

AB In adult rabbits, mid-diaphyseal segments of the radius or ulna were excised to produce defects greater than the critical size for spontaneous bone repair. The defects were enveloped in sleeves composed of nonbiodegradable expanded polyfluoroethylene (ePTFE), pore size 30, 60, 90 mum, and compared with sleeves of three biodegradable materials. Bone morphogenetic protein and associated noncollagenous bone matrix protein (BMP/NCP) or recombinant human morphogenetic protein (rhBMP-2) were implanted inside the sleeves. Albumin was implanted for a control system. Without intracompartmental BMP, only about 10%-15% of the defect was repaired by bone growth **extending** from the bone ends into the sleeves composed of ePTFE, pore size 30 mum. With sleeves with pore size 60 or 90 mum and intracompartmental BMP/NCP, 54%-96% regeneration occurred within 8 weeks after the operation. Sleeves of biodegradable nonimmunogenic materials such as polyorthoester (POE) and polylactic-polyglycollic acids (PLA/PGA) permitted 86%-98% restoration of bone continuity, but only when BMP was present in the lumen. With puncture holes (0.5 mm in diameter), implants of BMP/NCP in the 30-mum PTFE sleeve produced transmembrane external callus formation and bone regeneration to 147%. Sleeves composed of aorta first calcified, then induced complete intracompartmental bone regeneration. **Atelocollagen** sleeves incited a low-grade inflammatory cell reaction and did not promote complete regeneration. Under conditions presently undisclosed segments of the ulna bridged with ePTFE, were incompletely paired, even with intracompartmental BMP/NCP. Puncture holes of 0.5 mm admitted ingrowth of capillaries and introduced local conditions favorable for the response to BMP/NCP. BMP/NCP may promote profileration of nutrient vessels and differentiation of bone marrow stroma cells between the open bone ends. For further investigation, the hypothesis to be examined is that the optimum response to BMP/NCP and rhBMP-2 would emerge in compartments containing first a high concentration gradient and second proliferating perivascular cells.
CC Bones, joints, fasciae, connective and adipose tissue - Pathology 18006
Anatomy and Histology - Regeneration and transplantation 11107
Bones, joints, fasciae, connective and adipose tissue - Physiology and biochemistry 18004
Biochemistry studies - Proteins, peptides and amino acids 10064
IT Major Concepts

Skeletal System (Movement and Support)
IT Diseases
segmental diaphyseal defects: bone disease, compartmentalized, repair induction
IT Chemicals & Biochemicals
bone morphogenetic protein/noncollagenous bone matrix protein; expanded polyfluoroethylene: nonbiodegradable; polylactic-polyglycollic acids: biodegradable; polyorthoester: biodegradable; recombinant human morphogenetic protein
IT Miscellaneous Descriptors
bone regeneration; dystrophic calcification
ORGN Classifier
Leporidae 86040
Super Taxa
Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rabbit
Taxa Notes
Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

L54 ANSWER 15 OF 36 MEDLINE on STN
ACCESSION NUMBER: 1998045725 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9385958
TITLE: Evaluation of artecoll polymethylmethacrylate implant for soft-tissue augmentation: biocompatibility and chemical characterization.
COMMENT: Comment in: Plast Reconstr Surg. 1998 Oct;102(5):1786. PubMed ID: 9774076
Comment in: Plast Reconstr Surg. 1999 Jan;103(1):338-40. PubMed ID: 9915215
AUTHOR: McClelland M; Egbert B; Hanko V; Berg R A; DeLustro F
CORPORATE SOURCE: Collagen Corporation, Palo Alto, Calif. 94303, USA.
SOURCE: Plastic and reconstructive surgery, (1997 Nov) 100 (6) 1466-74.
Journal code: 1306050. ISSN: 0032-1052.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 20000303
Entered Medline: 19971218
AB Artecoll polymethylmethacrylate implant (Artecoll) is a combination of polymethylmethacrylate beads suspended in 3.5% atelocollagen and has been designed for use in soft-tissue augmentation applications. The biocompatibility and immunogenicity of Artecoll were evaluated to assess the safety of this product for use in the dermis. To characterize the collagen component, chemical analysis was performed including trypsin sensitivity, differential scanning calorimetry, and pepsin content. Particle size analysis was also performed on the polymethylmethacrylate beads. The ability of this material to elicit an immunologic response was measured in a sensitized and nonsensitized guinea pig intradermal model. In these studies, 24 guinea pigs were injected intradermally with either Artecoll or Zyderm, a bovine collagen product for soft-tissue augmentation. Six sites were evaluated for each material at 3, 7, and 28 days after injection. In the sensitized model, 60 guinea pigs were divided into five groups, and each group received a sensitizing dose (in conjunction with Freund's adjuvant) of Zyderm, Artecoll, or a

nonsensitizing dose of the same materials. The fifth group served as a nontreatment control. After the animals were sensitized, they were challenged with intradermal injections of various antigens to evaluate delayed type hypersensitivity reactions. Chemical characterization indicated polymethylmethacrylate beads of varying sizes, including many less than 35 microns, and a vehicle of **extensively** denatured and impure collagen. In vivo evaluations indicated that Artecoll elicited an immune response in guinea pigs, including delayed type hypersensitivity and antibody reactions. Histological assessment demonstrated particle phagocytosis and transepidermal elimination. Following immunization with Artecoll, guinea pigs were also found to be sensitized to pepsin, an impurity found in the collagen carrier. The biocompatibility of this material was compared with that of bovine dermal collagen (Zyderm collagen implant), which is widely used and accepted as biocompatible. The results of this evaluation indicate that Artecoll polymethylmethacrylate implant has the potential to elicit an immune response in humans, and polymethylmethacrylate beads are susceptible to phagocytosis and elimination.

CT Check Tags: Comparative Study
Adjuvants, Immunologic: CH, chemistry
Animals
Antibody Formation: IM, immunology
*Biocompatible Materials
Biocompatible Materials: AN, analysis
Biocompatible Materials: CH, chemistry
Biocompatible Materials: PD, pharmacology
Calorimetry, Differential Scanning
Cattle
Chemistry, Physical
*Collagen
Collagen: AN, analysis
Collagen: CH, chemistry
Collagen: IM, immunology
Collagen: PD, pharmacology
Disease Models, Animal
Evaluation Studies
Follow-Up Studies
Freund's Adjuvant: PD, pharmacology
Guinea Pigs
Hypersensitivity, Delayed: ET, etiology
Hypersensitivity, Delayed: IM, immunology
Immunization
Injections, Intradermal
Particle Size
Pepsin A: AN, analysis
Pepsin A: IM, immunology
Phagocytosis
*Polymethyl Methacrylate
Polymethyl Methacrylate: AN, analysis
Polymethyl Methacrylate: CH, chemistry
Polymethyl Methacrylate: PD, pharmacology
*Prostheses and Implants
Safety
Skin: DE, drug effects
Skin: IM, immunology
Skin: PA, pathology
Trypsin: CH, chemistry

RN 9007-34-5 (Collagen); 9007-81-2 (Freund's Adjuvant); 9011-14-7 (Polymethyl Methacrylate)

CN 0 (Adjuvants, Immunologic); 0 (Biocompatible Materials); **0**

(atelocollagen); EC 3.4.21.4 (Trypsin); EC 3.4.23.1 (Pepsin A)

L54 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:509610 HCAPLUS
DOCUMENT NUMBER: 125:151145
TITLE: Preparation of **sustained-release** injections for local anesthesia
INVENTOR(S): Kitamura, Masataka; Takei, Keiji
PATENT ASSIGNEE(S): Lederle Japan Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08143449	A2	19960604	JP 1994-307082	19941117
PRIORITY APPLN. INFO.:			JP 1994-307082	19941117

AB The sustained-release injections for local anesthesia are formulated by lidocaine, procaine, cocaine, and other local anesthetics and their salts with drug carriers e.g. collagen, gelatin, fibrinogen, fibrin, polylactate, polyglycolate, and/or polylactate-polyglycolate copolymer.
IC ICM A61K009-08
ICS A61K009-107; A61K031-16; A61K031-165; A61K031-245; A61K031-445; A61K031-46; A61K031-47; A61K047-34; A61K047-42
CC 63-6 (Pharmaceuticals)
ST **sustained release** injection local anesthetic prepn
IT Collagens, biological studies
Fibrinogens
Fibrins
Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **sustained-release** injections for local anesthesia)
IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**atelo**-, preparation of **sustained-release** injections for local anesthesia)
IT **Pharmaceutical dosage forms**
(injections, **sustained-release**, preparation of **sustained-release** injections for local anesthesia)
IT Anesthetics
(local, preparation of **sustained-release** injections for local anesthesia)
IT 50-36-2, Cocaine 59-46-1, Procaine 85-79-0, Dibucaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 137-58-6, Lidocaine 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 34346-01-5 51096-22-1D, Aminobenzoate, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **sustained-release** injections for local anesthesia)

L54 ANSWER 17 OF 36 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96272024 EMBASE
DOCUMENT NUMBER: 1996272024
TITLE: A new application of peptide drug delivery system to the brain.

AUTHOR: Koseki N.; Takemoto O.; Sasaki Y.; Maeda H.; Sano A.; Fujioka K.; Sato A.; Miyata T.; Muhammad A.K.M.G.; Yoshimine T.; Hayakawa T.
CORPORATE SOURCE: Fomulation Research Laboratories, Research Center, Sumitomo Pharmaceuticals Co. Ltd.,Ibaraki, Osaka 567, Japan
SOURCE: Proceedings of the Controlled Release Society, (1996) -/23 (605-606).
ISSN: 1022-0178 CODEN: 58GMAH
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
CT Medical Descriptors:
*drug brain level
*drug formulation
*drug release
animal experiment
animal tissue
brain
cat
caudate nucleus
conference paper
controlled study
drug distribution
drug half life
intracerebral drug administration
nonhuman
*drug delivery system
***sustained release preparation**
drug implant
Drug Descriptors:
*nerve growth factor: AD, drug administration
*nerve growth factor: CR, drug concentration
*nerve growth factor: DV, drug development
*nerve growth factor: PR, pharmaceutics
*nerve growth factor: PK, pharmacokinetics
atelocollagen
peptide
RN (nerve growth factor) 9061-61-4

L54 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 1996:50763 HCAPLUS
DOCUMENT NUMBER: 124:97792
TITLE: **Sustained-release** antitumor hydrogels containing camptothecins
INVENTOR(S): Kurono, Yukihisa; Kamimura, Kunio; Ikeda, Ken
PATENT ASSIGNEE(S): Yakult Honsha Kk, Japan; Daiichi Seiyaku Co
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 07277981 A2 19951024 JP 1994-107359 19940412
PRIORITY APPLN. INFO.: JP 1994-107359 19940412
AB The antitumor prepns. are hydrogels prepared by impregnation of a collagen-2-hydroxyethyl methacrylate (I) copolymer carrier with camptothecin derivs. A solution of atelocollagen in an aqueous HCl was mixed with an aqueous solution of CPT 11 and I, and the mixture was further treated with ethylene glycol, an aqueous (NH4)2S2O8 solution, and an aqueous Na2S2O5 solution at 37° for 3 h to give a sustained-release hydrogel. The hydrogel was administered to healthy mice. Plasma level of SN-38 (metabolite of CPT 11) was gradually decreased from 0.5 μg/mL to <0.1 μg/mL over 5 days, while the level after a one-shot injection of an aqueous CPT 11 solution decreased 0.05 μg/mL within a day. The hydrogel also showed excellent antitumor effect on mice bearing Ehrlich cells.
IC ICM A61K031-47
ICS A61K009-52; A61K047-32; A61K047-42
ICA A61K035-78; C07D491-22
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST collagen methacrylate hydrogel antitumor carrier; camptothecin carrier collagen methacrylate hydrogel; **sustained release** antitumor carrier hydrogel
IT Collagens, biological studies
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(copolymers with 2-hydroxyethyl methacrylate; **sustained-release** antitumor hydrogels containing camptothecins using collagen-hydroxyethyl methacrylate copolymer carriers)
IT Neoplasm inhibitors
(**sustained-release** antitumor hydrogels containing camptothecins using collagen-hydroxyethyl methacrylate copolymer carriers)
IT **Collagens, biological studies**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**atelo-**, copolymers with 2-hydroxyethyl methacrylate; **sustained-release** antitumor hydrogels containing camptothecins using collagen-hydroxyethyl methacrylate copolymer carriers)
IT 78287-27-1, 7-Ethylcamptothecin 86639-52-3, 7-Ethyl-10-hydroxycamptothecin 97682-44-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**sustained-release** antitumor hydrogels containing camptothecins using collagen-hydroxyethyl methacrylate copolymer carriers)
IT 868-77-9DP, 2-Hydroxyethyl methacrylate, copolymers with collagens
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**sustained-release** antitumor hydrogels containing camptothecins using collagen-hydroxyethyl methacrylate copolymer carriers)

L54 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:913631 HCAPLUS
DOCUMENT NUMBER: 123:296662
TITLE: Collagen-based injectable drug delivery system and its use

INVENTOR(S): Rosenblatt, Joel S.; Berg, Richard A.
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: Can. Pat. Appl., 44 pp.
CODEN: CPXXEB
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2140053	AA	19950810	CA 1995-2140053	19950111
CA 2140053	C	20000404		
AU 9510295	A1	19950817	AU 1995-10295	19950119
AU 701743	B2	19990204		
EP 671165	A2	19950913	EP 1995-101589	19950206
EP 671165	A3	19951122		
EP 671165	B1	20010418		
R: CH, DE, FR, GB, IT, LI				
JP 08034747	A2	19960206	JP 1995-20798	19950208
US 5807581	A	19980915	US 1995-537073	19950929

PRIORITY APPLN. INFO.: US 1994-193600 A 19940209

AB Drugs delivered in a substained manner from an in vivo depot which is formed from a collagen-based injectable composition The injectable composition is fluid when injected but undergoes crosslinking in situ to form a crosslinked collagen matrix which encloses the drug to be released. The composition also includes a flexible chain polymer which is similarly charged to the precrosslinking collagen. This flexible chain polymer is enclosed in the matrix as well when the matrix forms and alters the effective porosity of the matrix. The drug diffuses out of the matrix at a rate which depends upon the matrix's effective porosity.

IC ICM A61K047-00
ICS A61K009-22
CC 63-6 (Pharmaceuticals)
ST **sustained release** injection collagen
IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**atelo-**, collagen-based injectable drug delivery system)
IT **Pharmaceutical dosage forms**
(injections, **sustained-release**; collagen-based injectable drug delivery system)

L54 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:240966 HCAPLUS
DOCUMENT NUMBER: 118:240966
TITLE: **Sustained-release** transdermal tapes containing hormones as wound healing enhancers
INVENTOR(S): Osada, Akihiko; Kadota, Keiichi; Fujioka, Takaharu; Sano, Akihiko; Maeda, Yoshiho; Kajiwara, Masako
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan; Koken Kk
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 05043453 A2 19930223 JP 1991-207873 19910820
PRIORITY APPLN. INFO.: JP 1991-207873 19910820
AB A sustained-release transdermal tape is prepared by adding a physiol. active agent to a carrier of collagen, optionally with albumins, gelatin, chitin, poly(lactic acid), poly(glycolic acid), or copolymer thereof. The physiol. active agent may be growth hormone, insulin-like growth hormone-1, fibroblast growth hormone, growth hormone derived from blood plasma, α- and β-transforming growth factors, insulin, neurotrophic factors, and epithelial cell growth factors. For example, human growth factor and human serum albumin were added to an atelocollagen soln, freeze-dried, mixed with water to adjust the collagen concentration to 10 % and made into a transdermal film.
IC ICM A61K009-70
ICS A61K009-14; A61K009-70; A61K037-02; A61K037-26; A61K037-36; A61K045-00; A61K047-34; A61K047-36; A61K047-42
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 2
IT **Collagens, biological studies**
RL: BIOL (Biological study)
(**atelo**-, wound healing transdermal tape containing)

L54 ANSWER 21 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 2
ACCESSION NUMBER: 1993:497271 BIOSIS
DOCUMENT NUMBER: PREV199396121278
TITLE: Epithelial cell kinetics with **atelocollagen** membranes: A study in rats.
AUTHOR(S): Numabe, Yukihiro [Reprint author]; Ito, Hiroshi; Hayashi, Hideaki; Ryder, Mark I.; Kamoi, Kyuichi
CORPORATE SOURCE: Dep. Periodontol., Sch. Dentistry Tokyo, Nippon Dental Univ., 2-3-16 Fujimi-cho, Chiyoda-ku, Tokyo 102, Japan
SOURCE: Journal of Periodontology, (1993) Vol. 64, No. 8, pp. 706-712.
CODEN: JOPRAJ. ISSN: 0022-3492.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 1993
Last Updated on STN: 6 Nov 1993
AB A recent development in guided tissue regeneration procedures is the use of resorbable membranes, which eliminate the need for subsequent surgical removal. In this study we performed flap surgery in rats with (experimental) or without (control) implantation of one of the newer materials, **atelocollagen.** We observed the gingival epithelial cell kinetics using 3H-thymidine and examined the **extent** of gingival epithelium migration. Histological observations at day 1 on the experimental side demonstrated regenerated epithelium apposed to the collagen membrane with an intervening layer of necrotic tissues and/or fibrinous exudate. There was no observable proliferation of regenerated epithelium toward the root apex. On day 14, the regenerated epithelium migrated apically along the treated root surface in the control group. By contrast, on day 14 in the experimental group, the regenerated epithelium contacted the root surface at the cemento-enamel junction (CEJ). Apical to the CEJ, there was new cementum formation with inserting connective tissue fibers. Autoradiographs from day 1 experimental sides demonstrated labeled cells in the basal cell layers from oral, crevicular, and junctional epithelium. From day 1 to day 5, labeling indices of oral epithelium and regenerating crevicular epithelium on experimental sides were lower than on control sides. These histological and autoradiographic findings suggest that **atelocollagen** membrane inhibits apical

migration of regenerating epithelium and accelerates connective tissue reattachment in part by inhibiting the mitotic function of basal epithelial cells in early stages of wound healing.

CC Microscopy - Histology and histochemistry 01056
Cytology - Animal 02506
Radiation biology - Radiation and isotope techniques 06504
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Anatomy and Histology - Experimental anatomy 11104
Anatomy and Histology - Microscopic and ultramicroscopic anatomy 11108
Dental biology - Physiology and biochemistry 19004
Dental biology - Pathology 19006

IT Major Concepts
Cell Biology; Dental and Oral System (Ingestion and Assimilation)

IT Chemicals & Biochemicals
THYMIDINE

IT Miscellaneous Descriptors
DENTAL MODELS; REGRESSION ANALYSIS

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Muridae
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 50-89-5 (THYMIDINE)

L54 ANSWER 22 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1994:18657 BIOSIS
DOCUMENT NUMBER: PREV199497031657
TITLE: A bilayer artificial skin composed of collagen matrix.
AUTHOR(S): Kawai, Toshio [Reprint author]; Ohno, Sumio [Reprint author]; Terayama, Yoshiyasu [Reprint author]; Natsume, Hideshi [Reprint author]; Sugibayashi, Kenji [Reprint author]; Morimoto, Yasunori [Reprint author]; Shibata, Toshikatsu
CORPORATE SOURCE: Dep. Pharmaceutics, Fac. Pharmaceutical Sci., Josai Univ. 1-1 Keyakidai, Sakado, Saitama 350-02, Japan
SOURCE: Skin Research, (1993) Vol. 35, No. 4, pp. 471-476. CODEN: HIFUAG. ISSN: 0018-1390.
DOCUMENT TYPE: Article
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 25 Jan 1994
Last Updated on STN: 18 Nov 1994

AB In order to evaluate and develop a wound dressing (artificial skin) which slowly releases drug(s), **atelocollagen** was cross-linked by glutaraldehyde (GA) or both GA and octylaldehyde (OA) to make two kinds of membrane and each of the resulting membrane was piled on silicone adhesive to finally make artificial skin (former dressing was the same to one by

Yannas), and their usefulness was compared by a histological point of view. No difference was found in shrinking of the wound treated by both artificial skins, and the **extent** of the shrinking was much less than that for the open wound. Histological observation showed that the cross-linked membrane by both GA and OA repaired the dermis and formed the pseudo-dermis at a similar rate as found in the membrane treated by GA alone. These findings suggest a usefulness of the membrane by both GA and OA as well as the GA-treated membrane for an artificial skin.

CC Biochemistry studies - General 10060
Anatomy and Histology - Regeneration and transplantation 11107
Anatomy and Histology - Microscopic and ultramicroscopic anatomy 11108
Pathology - Therapy 12512
Integumentary system - General and methods 18501
Integumentary system - Pathology 18506
Temperature - Thermopathology 23007

IT Major Concepts
Biochemistry and Molecular Biophysics; Integumentary System (Chemical Coordination and Homeostasis); Morphology; Pathology; Physiology

IT Chemicals & Biochemicals
GLUTARALDEHYDE; OCTYLALDEHYDE

IT Miscellaneous Descriptors
ATELOCOLLAGEN; BURN THERAPY; GLUTARALDEHYDE; GRAFT; HISTOLOGY; OCTYLALDEHYDE

RN 111-30-8 (GLUTARALDEHYDE)
124-13-0 (OCTYLALDEHYDE)

L54 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1991:566675 HCAPLUS
DOCUMENT NUMBER: 115:166675
TITLE: **Sustained-release** pharmaceutical powders containing soluble collagen (derivatives) as carriers
INVENTOR(S): Myata, Teruo; Kudome, Satoru
PATENT ASSIGNEE(S): Koken Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03093716	A2	19910418	JP 1989-230421	19890907
JP 2789115	B2	19980820		
JP 10182499	A2	19980707	JP 1998-48559	19980216
JP 3240593	B2	20011217		

PRIORITY APPLN. INFO.: JP 1989-230421 A3 19890907

AB Soluble collagen and/or soluble collagen derivative solns. or dispersions containing ≥1 active ingredient(s) are spray-dried to manufacture the title powders (average particle size 0.1-50 μm). The powders are useful for ophthalmic treatment, etc. An aqueous solution (pH 9) containing 2.5 g bovine atherocollagen was treated with 1 g succinic anhydride to give succinic acid-modified collagen. An aqueous 1% the modified collagen solution (1 L) was mixed with 500 μm gentamycin (I) and the mixture was spray-dried at 60° to manufacture powders (average particle size 2.5 μm), which were applied to eyes of rabbits to show I controlled-release property. The concentration of I in the

tear was kept higher than with I injection even 6 h after.
IC ICM A61K009-16
ICS A61K047-42
CC 63-6 (Pharmaceuticals)
ST collagen pharmaceutical powder **sustained release**
IT Collagens, biological studies
RL: BIOL (Biological study)
(water-soluble, pharmaceutical powders containing, **sustained-release**)
IT **Collagens, biological studies**
RL: BIOL (Biological study)
(**atelo**-, pharmaceutical powders containing, **sustained-release**)
IT **Pharmaceutical dosage forms**
(powders, **sustained-release**, containing water-soluble collagen (derivs.))
IT 108-30-5DP, Succinic acid anhydride, reaction product with collagen
RL: PREP (Preparation)
(preparation of, pharmaceutical powders containing, **sustained-release**)

L54 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:520036 HCAPLUS
DOCUMENT NUMBER: 115:120036
TITLE: **Sustained-release** preparation for administration into the brain
INVENTOR(S): Hayakawa, Toru; Yoshimine, Toshiki; Fujioka, Keiji; Takada, Yoshihiro; Sasaki, Yoshio; Irie, Tsunemasa; Fukushima, Nobuyuki
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan; Koken Co., Ltd.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 412554	A2	19910213	EP 1990-115389	19900810
EP 412554	A3	19910925		
EP 412554	B1	19941102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 03163032	A2	19910715	JP 1990-210615	19900808
JP 3187410	B2	20010711		
ES 2066062	T3	19950301	ES 1990-115389	19900810
PRIORITY APPLN. INFO.:			JP 1989-208484 A	19890810

AB A sustained-release preparation for the treatment of diseases of the brain contains a pharmaceutically active substance incorporated into a biodegradable carrier (e.g., collagen, gelatin). The active substance may be an immunostimulator, neurotrophic factor, brain peptide, anticancer agent, etc. The preparation may be implanted in the brain. Thus, a bar-like sustained-release preparation including nerve growth factor (NGF) and atelocollagen was prepared and inserted into the left dorsal hippocampus of a Mongolian gerbil. Four days following bilateral common carotid artery occlusion, various areas of the brain were examined The disintegration of pyramidal cells was little observed not only in the inserted hippocampus, but also in the opposite hippocampus. The NGF concentration in the inserted part was

higher than that in the opposite part; NGF concentration was highest in the striatum, and the next was the occipital part of the cerebral cortex.

IC ICM A61K009-22
ICS A61K009-20

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 15

ST brain **sustained release** pharmaceutical; implant **sustained release** pharmaceutical brain; nerve growth factor implant brain

IT Peptides, biological studies
RL: BIOL (Biological study)
(brain, **sustained-release** pharmaceutical of, for cerebral disease treatment)

IT Brain, composition
(hippocampus factor, **sustained-release** pharmaceutical containing, for cerebral disease treatment)

IT Blood-brain barrier
(pharmaceutical transport across, **sustained-release**)

IT Antibiotics
Immunostimulants
Neoplasm inhibitors
Animal growth regulators
Interferons
RL: BIOL (Biological study)
(**sustained-release** pharmaceutical of, for cerebral disease treatment)

IT Antibodies
RL: BIOL (Biological study)
(to brain peptides, **sustained-release** pharmaceutical of, for cerebral disease treatment)

IT **Collagens, biological studies**
RL: BIOL (Biological study)
(**atelo**-, as pharmaceutical carriers, for cerebral disease treatment)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukins, **sustained-release** pharmaceutical of, for cerebral disease treatment)

IT Neurohormones
RL: BIOL (Biological study)
(neurotransmitters, **sustained-release** pharmaceutical of, for cerebral disease treatment)

IT Animal growth regulators
RL: BIOL (Biological study)
(neurotropic, **sustained-release** pharmaceutical of, for cerebral disease treatment)

IT **Pharmaceutical dosage forms**
(**sustained-release**, for cerebral disease treatment, with biodegradable carrier)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(tumor necrosis factor, **sustained-release** pharmaceutical of, for cerebral disease treatment)

IT 106096-93-9, Basic fibroblast growth factor
RL: BIOL (Biological study)
(**sustained release** pharmaceutical of, for cerebral disorder treatment)

IT 9011-97-6, Cholecystokinin 9061-61-4, Nerve growth factor 11000-17-2, Vasopressin 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal

growth factor
RL: BIOL (Biological study)
(**sustained-release** pharmaceutical of, for cerebral disease treatment)

L54 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:484907 HCAPLUS
DOCUMENT NUMBER: 113:84907
TITLE: Biocompatible materials for preparation of prosthetics and microcapaules
INVENTOR(S): Koide, Mikio; Konishi, Atsushi
PATENT ASSIGNEE(S): Terumo Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02001287	A2	19900105	JP 1987-327316	19871225
JP 03011786	B4	19910218		
PRIORITY APPLN. INFO.:			JP 1986-309728	19861225
			JP 1986-309729	19861225
			JP 1987-281126	19871109

AB The title biocompatible materials are mixts. of degenerated collagen (atelocollagen from bovine dermal collagen treated at 37-90° after removal of antigen group) and water-soluble polysaccharides (acid mucopolysaccharides e.g. chondroitin sulfate, heparan sulfate, alginic acid, hyaluronic acid, etc.), with coacervate structure. Prosthetics and microcapsules (e.g. for cell growth factors, etc.) prepared by these materials can be used in medicine, cosmetics and food additives, with good biocompatibility. Thus, biocompatible coacervates were prepared by atelocollagen (heated at 60°) and chondroitin 6-sulfate mixture (pH 3.0-5.0). Microcapsules containing vitamin B12 were also prepared by using the coacervates, and their solution rate and sustained-release properties were tested in vitro.

IC ICM A61L027-00
ICS A61K009-50; A61K047-36; A61K047-42; A61L031-00; A61L033-00
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 17, 62
IT Mucopolysaccharides, biological studies
RL: PREP (Preparation)
(acid, biocompatible coacervates prepared by **atelocollagen** and, for preparation of drug microcapsules and prosthetics)
IT **Collagens, biological studies**
RL: PREP (Preparation)
(**atelo**-, biocompatible coacervates prepared by acid mucopolysaccharides and, for preparation of drug microcapsules and prosthetics)
IT **Pharmaceutical dosage forms**
(microcapsules, **sustained-release**, biocompatible coacervates for preparation of)
IT 9005-49-6, Heparin, biological studies 25322-46-7
RL: BIOL (Biological study)
(biocompatible coacervates prepared by **atelocollagen** and, for preparation of drug microcapsules and prosthetics)

L54 ANSWER 26 OF 36 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1990-240881 [32] WPIX
DOC. NO. CPI: C1990-104114
TITLE: Microcapsules for cosmetic, pharmaceutical or food compsns. - prepared using solution of atelo-collagen and poly holoside, e.g. glucosamine-glycan cpds..
DERWENT CLASS: B07 D13 D21
INVENTOR(S): ANDRY, M; BUFFEVANT, C; HUC, A; LEVY, M; ANDRY, M C; LEVY, M C
PATENT ASSIGNEE(S): (BIOE-N) BIOETICA; (COLE-N) COLETICA; (BIOE-N) BIOETICA SA
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 381543	A	19900808	(199032)*		16
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
FR 2642329	A	19900803	(199038)		
AU 9048864	A	19900809	(199039)		
CA 2009065	A	19900731	(199042)		
JP 02229111	A	19900911	(199042)		
AU 633866	B	19930211	(199313)		
EP 381543	B1	19930526	(199321)	EN	17
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
DE 69001683	E	19930701	(199327)		
ES 2058827	T3	19941101	(199444)		
US 5395620	A	19950307	(199515)		9
JP 2534921	B2	19960918	(199642)		10
US 5622656	A	19970422	(199722)		10
CA 2009065	C	19990824	(200001)	EN	
KR 163171	B1	19981201	(200032)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 381543	A		EP 1990-400030	19900105
FR 2642329	A		FR 1989-1221	19890131
JP 02229111	A		JP 1990-21927	19901031
AU 633866	B		AU 1990-48864	19900129
EP 381543	B1		EP 1990-400030	19900105
DE 69001683	E		DE 1990-601683	19900105
			EP 1990-400030	19900105
ES 2058827	T3		EP 1990-400030	19900105
US 5395620	A	CIP of	US 1989-336711	19890412
		Cont of	US 1991-749909	19910826
			US 1993-74701	19930608
JP 2534921	B2		JP 1990-21927	19900131
US 5622656	A	CIP of	US 1989-336711	19890412
		Cont of	US 1991-749909	19910826
		Div ex	US 1993-74701	19930608
			US 1994-328903	19941025
CA 2009065	C		CA 1990-2009065	19900131
KR 163171	B1		KR 1990-1111	19900131

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 633866	B	Previous Publ.	AU 9048864

DE 69001683	E Based on	EP 381543
ES 2058827	T3 Based on	EP 381543
JP 2534921	B2 Previous Publ.	JP 02229111
US 5622656	A Div ex	US 5395620

PRIORITY APPLN. INFO: US 1989-336711 19890412; FR 1989-1221 19890131

AN 1990-240881 [32] WPIX

AB EP 381543 A UPAB: 19970502

The use of a solution of **atelocollagen** and polyholosides, eg. glycosaminoglycans (GAGs) for the mfr. of microcapsules which pref. contain an active principle, especially of the cosmetic, pharmaceutical or edible type, is claimed. Also claimed are microcapsules which comprise a mixed wall of crosslinked ateocollagen and polyholosides, eg. GAGs.

The GAGs may be eg. chondroitin 4-sulphate, chondroitin 6-sulphate, dermatan sulphate, heparan sulphate, keratan sulphate or heparin. In the preparation of the microcapsules, there may be used a crosslinking agent, eg. terephthaloyl chloride, citric acid or succinic anhydride, a hydrophobic liquid, eg. cyclohexane or CHCl3, a buffer solution for dissolving polyholosides containing eg. NaOH, Na2CO3, Sodium acetate, sodium citrate or sodium and potassium phosphates and a solution for dissolving the **atelocollagen**, eg. aqs. 0.1M acetic acid.

USE/ADVANTAGE - The microcapsules by virtue of the presence of **atelocollagen** have very low antigenicity and perfect biodegradability. In pharmaceutical compsns., the microcapsules make it possible, when administered orally, to mask the taste of the active principle and to provide protection in the stomach or produce a delayed effect by virtue of resistance to the gastric juices. The microcapsules also make it possible to protect delicate substances such as essential oils which may form part of a compsn. of foods. @(16pp Dwg.No.0/1)

ABEQ EP 381543 B UPAB: 19931114

Use of a solution of **atelocollagen** and polyholosides, for example glycosaminoglycans, for the manufacture of microcapsules which preferably contain an active principle, especially of the cosmetic, pharmaceutical or edible type.

Dwg.0/0

ABEQ US 5395620 A UPAB: 19950425

Microcapsule comprises a cross-linked outer wall surrounding a filled inner space, the outer wall resulting from crosslinking between mols. of atelo collagen (ATC) and polyholoside. Opt. the microcapsule contains an active cpd. such as a cosmetic, pharmaceutical or food cpd.

The polyholoside is pref. a glycosaminoglycan esp. chondroitin 4- or 6-sulphate, dermatan sulphate, heparin sulphate, keratan sulphate or heparin (of mol. wt. 2000-10000). The filled inner space comprises a mixt. of ATC and polyholoside.

USE/ADVANTAGE - The microcapsules are biocompatible by virtue of the presence of atelo collagen which has the advantageous properties of collagen such as very low antigenicity and biodegradability and are suitable for mfr. of cosmetic, pharmaceutical or food compsns.

Dwg.0/1

ABEQ US 5622656 A UPAB: 19970530

A process for the manufacture of microcapsules, which comprises the following successive steps:

(a) preparing a solution of **atelocollagen**,

(b) preparing a solution of polyholoside by dissolving the polyholoside in an aqueous buffer solution whose pH is adjusted so that, after mixing with the solution of **atelocollagen**, the pH of the mixture is between 5.5 and 10,

(c) mixing the solution of **atelocollagen** with the solution of polyholoside to form a homogeneous solution of **atelocollagen**

and polyholoside having a pH between 5.5 and 10,

(d) forming an emulsion with the solution of **atelocollagen** and polyholoside, as a dispersed phase in a hydrophobic liquid forming the continuous phase, in which the **atelocollagen** and the polyholoside are essentially insoluble, and

(e) mixing a crosslinking solution of a crosslinking agent containing reactive groups capable of simultaneously reacting with acylatable groups of the **atelocollagen** and the polyholoside with the resulting emulsion, thereby causing an interfacial and simultaneous crosslinking reaction of the **atelocollagen** and of the polyholoside, for a period of time sufficient to form microcapsules comprising a crosslinked outerwall surrounding a filled inner space, said outerwall resulting from a crosslinking between molecules of **atelocollagen** and polyholoside.

Dwg.1/1

L54 ANSWER 27 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1990:452923 BIOSIS
DOCUMENT NUMBER: PREV199090103563; BA90:103563
TITLE: INTRACORDAL INJECTION OF **ATELOCOLLAGEN** FOR VOCAL REHABILITATION.
AUTHOR(S): TAKAYAMA E [Reprint author]; FUKUDA H; KAWAIDA M; KAWASAKI Y; SAKO T; OTSUKI J; INOUE Y; TOMIZAWA I
CORPORATE SOURCE: DEP OTOLARYNGOL, SAISEIKAI CENT HOSP, TOKYO
SOURCE: Journal of the Japan Broncho-Esophagological Society, (1990) Vol. 41, No. 3, pp. 196-201.
CODEN: NKSGAH. ISSN: 0029-0645.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: JAPANESE
ENTRY DATE: Entered STN: 7 Oct 1990
Last Updated on STN: 4 Jan 1991

AB Voice disorders to which intracordal injection for vocal rehabilitation can be applied have been expanded by the introduction of collagen. Attention has focused on intracordal injection as an effective method for rehabilitation. This method is applicable not only to unilateral vocal paralysis, but also cases of insufficient glottal closure, such as sulcus vocalis and vocal atrophy. Injection of 3% **atelocollagen** was conducted in 9 cases of sulcus vocalis and one case of postoperative vocal fold scaring. These voice disorders show insufficient glottal closure and problem of vocal fold flexibility. Following results have been obtained with the study of 10 cases of such disorders: (1) In 80% of cases, vocal fold vibration, hoarseness and tiredness during phonation were proved. (2) In cases where the symptoms improved, the maximum **sustained** phonation time was prolonged. However, the mean flow rate decreased in some cases and increased somewhat in others. (3) In cases where the symptoms were aggravated, the injection of DMPS had been carried out within one year previous to the operation.

CC Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Anatomy and Histology - Surgery 11105
Pathology - Therapy 12512
Respiratory system - General and methods 16001
Respiratory system - Pathology 16006
Sense organs - Deafness, speech and hearing 20008
Pharmacology - Clinical pharmacology 22005
Pharmacology - Respiratory system 22030
Routes of immunization, infection and therapy 22100
Toxicology - Pharmacology 22504

IT Major Concepts
Pharmacology; Pulmonary Medicine (Human Medicine, Medical Sciences); Sense Organs (Sensory Reception)
IT Miscellaneous Descriptors
HUMAN 2 3 DIMERCAPTO-1-PROPANESULFONIC ACID VOCAL ATROPHY VOCAL PARALYSIS SULCUS VOCALIS SURGERY
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 74-61-3 (2 3-DIMERCAPTO-1-PROPANESULFONIC ACID)

L54 ANSWER 28 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1991:114648 BIOSIS
DOCUMENT NUMBER: PREV199191062038; BA91:62038
TITLE: CUTANEOUS COLLAGEN METABOLISM IN-VITRO FIBRILLOGENESIS IN VARIOUS GELS IN-VIVO CHANGES AND RELATED BIOREACTIONS.
AUTHOR(S): SOMEDA Y [Reprint author]
CORPORATE SOURCE: DEP DERMATOL, OSAKA CITY UNIV MED SCH
SOURCE: Journal of the Osaka City Medical Center, (1990) Vol. 39, No. 1, pp. 101-140.
CODEN: OIGZDE. ISSN: 0386-4103.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: JAPANESE
ENTRY DATE: Entered STN: 27 Feb 1991
Last Updated on STN: 27 Feb 1991

AB Collagen solution used clinically for subcutaneous implants, wound dressings, and artificial vitreum consists of **atelocollagen** obtained by solubilization with pepsin and purification of animal corium and tendon. When warned to 37° C, collagen fibrils are arranged in a three-dimensional network and become a collagen gel (gel). Administration of collagen solution into living organisms is considered to provide an experimental model for evaluation of dermal collagen metabolism in which changes in the collagen administered as well as responses of the endogenous collagen, matrix, and cells of the body can be observed. The process of fibrillogenesis was examined electron microscopically in vitro. Collagen solutions derived from bovine corium (Kokencellgen) and porcine Achilles tendon (Nitta Gelatin Cellmatrix) were used. In vivo, collagen solutions derived from bovine corium (Koken **Atelocollagen** Implant and Zyderm) in various doses were administred subcutaneously to rats and mice, and the injection sites were examined at various intervals for up to 6 months. The following results were obtained. 1) In vitro fibrillogenesis: with Kokencellgen, fine fibrous materials aggregated in the same direction and formed a fibril, which increased in length and thickness as more fine fibrous materials accumulated. Clear striation appeared when filaments constituting the fibril had been densely and regularly arranged. With Nitta Gelatin Cellmatrix, aggregates showing striation appeared early and these aggregates formed a fibril by aligning or interwining. Materials closer to native collagen fibrils were obtained with Kokencellgen than with Nitta Gelatin Cellmatrix. 2) In vivo kinetics and bioresponses: in the group subjected to a 0.5 ml Koken **Atelocollagen** Implant, calcium deposits were observed in the gel at most injection sites and foreign body granuloma formed in the surrounding areas. Under the electron microscope, calcium deposits were noted both in the gel-derived collagen fibrils and in the host-derived collagen fibers. In the animals subjected to a 0.05-0.2 ml Koken

Atelocollagen Implant, the frequency of calcium deposition and foreign body granuloma increased, dose dependently. In the gels with no calcium deposits, fibroblasts and capillaries entered the entire gel and a gradual absorption followed. Calcification was observed infrequently in Zyderm, and early penetration of fibroblasts and capillaries into the gel occurred. These results clarify to some **extent** in vivo changes of collagen and the relation to calcification and foreign body reactions.

CC Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Minerals 10069
Biophysics - Bioengineering 10511
Anatomy and Histology - Surgery 11105
Pathology - Inflammation and inflammatory disease 12508
Pathology - Therapy 12512
Metabolism - Minerals 13010
Metabolism - Proteins, peptides and amino acids 13012
Bones, joints, fasciae, connective and adipose tissue - Physiology and biochemistry 18004
Integumentary system - Physiology and biochemistry 18504
Integumentary system - Pathology 18506
In vitro cellular and subcellular studies 32600

IT Major Concepts
Cell Biology; Integumentary System (Chemical Coordination and Homeostasis); Metabolism; Methods and Techniques; Pathology; Skeletal System (Movement and Support); Surgery (Medical Sciences)

IT Miscellaneous Descriptors
RAT MOUSE IMPLANTS WOUND DRESSINGS CALCIFICATION FOREIGN BODY GRANULOMA

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L54 ANSWER 29 OF 36 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1989-222113 [31] WPIX
DOC. NO. CPI: C1989-098644
TITLE: Sustained release formulations - containing collagen and active ingredient, having release rate controlled by incorporation of organic acid cpd..
DERWENT CLASS: B04 B07
INVENTOR(S): FUJIOKA, K; MAEDA, M; SASAKI, Y; SATO, S; TAKADA, Y; TAMURA, N
PATENT ASSIGNEE(S): (SUMU) SUMITOMO PHARM CO LTD; (KOKE) KOKEN KK; (KOKE) KOKEN CO LTD
COUNTRY COUNT: 16
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 326151	A	19890802	(198931)*	EN	13
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
JP 02000710	A	19900105	(199007)		
EP 326151	B1	19930616	(199324)	EN	17
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
DE 68907066	E	19930722	(199330)		
US 5236704	A	19930817	(199334)		11
ES 2058351	T3	19941101	(199444)		
CA 1338839	C	19970114	(199714)		

JP 2641755 B2 19970820 (199738) 8

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 326151	A	EP 1989-101428	19890127
JP 02000710	A	JP 1989-20194	19890130
EP 326151	B1	EP 1989-101428	19890127
DE 68907066	E	DE 1989-607066	19890127
		EP 1989-101428	19890127
US 5236704	A	US 1989-302476	19890127
ES 2058351	T3	EP 1989-101428	19890127
CA 1338839	C	CA 1989-589427	19890127
JP 2641755	B2	JP 1989-20194	19890130

FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 68907066	E Based on	EP 326151
ES 2058351	T3 Based on	EP 326151
JP 2641755	B2 Previous Publ.	JP 02000710

PRIORITY APPLN. INFO: JP 1988-20459 19880129; JP 1989-20194 19890130

AN 1989-222113 [31] WPIX

AB EP 326151 A UPAB: 19940517

A sustained release formulation is claimed comprising an active ingredient (I) and collagen as a carrier, characterised in that it contains at least one organic acid cpd. (II) or an acid anhydride or ester capable of qenerating (II) through hydrolysis.

(I) may be e.g. interleukins, interferons, colony-stimulating factors, growth hormone, calcitonin, growth hormone-releasing factors (GRFs) leutinising hromone-releasing hormone, somatostatin, somatomedin, nerve growth factor, epidermal growth factor, transforming growth factor, fibroblast growth factor, erythropietin, platelet-derived growth factor, tissue plasminogen activator or urokinase. (I) may be e.g. aspartic acid, glutamic acid, qlycine, alanine, citric acid, ascorbic acid, tartaric acid, succinic acid or acetic acid. The collagen is pref. **atelocollagen.**

USE/ADVANTAGE - With the formulation, the release rate of (I) can be adjusted as desired by virtue of the addition of (II). In addition the carrier is colalqenNcollagen which is highly biocompatible and biodeqradable. Accordingly, the formulation is safe to use and especially suitable for the treatment of patients.

Dwg.0/4

ABEQ EP 326151 B UPAB: 19931116

1. A sustained release formulation which is suitable for human and veterinary use, comprising bioactive proteins and peptides as an active ingredient and collagen as a carrier, characterised in that it comprises at least one pharmaceutically or veterinary acceptable organic acidic compound, or aqueous solution of which has a pH below 7, or an acid anhydride or ester capable of generating one of the above-mentioned organic acidic compounds through hydrolysis.

Dwg.0/4

USE/ADVANTAGE - With the formulation, the release rate of (I) can be adjusted as desired by virtue of the addn. of (II). In addn. the carrier is colalqenNcollagen which is highly biocompatible and biodegradable. Accordingly, the formulation is safe to use and esp. suitable for the

treatment of patients.
0/4

ABEQ US 5236704 A UPAB: 19931119
Controlling release rate or release profile of an active ingredient from a sustained compsn. comprising collagen carrier and a bioactive protein or peptide as an active ingredient comprises incorporating 1-50 wt.% of at least one aminoacid of pH less than 7 when dissolved in water, into the compsn..
The collagen is pref. **atelocollagen** and the bioactive cpd. is a cytokine, hormone, hormone-releasing factor, hormone release-inhibiting factor, growth factor or enzyme. The aminoacid is e.g. aspartic acid, glutamic acid, glycine or alanine.
USE/ADVANTAGE - For controlled release of active agents for human or veterinary use.
Dwg.0/4

L54 ANSWER 30 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 4

ACCESSION NUMBER: 1989:402218 BIOSIS
DOCUMENT NUMBER: PREV198988071643; BA88:71643
TITLE: EFFECTS OF **ATELOCOLLAGEN** ON THE WOUND HEALING REACTION FOLLOWING PALATAL GINGIVECTOMY IN RATS.
AUTHOR(S): MINABE M [Reprint author]; KODAMA T; HORI T; WATANABE Y
CORPORATE SOURCE: DEP PERIODONTOL, KANAGAWA DENT COLL, INAOKO-CHO 82, YOKOSUKA, KANAGAWA, JPN
SOURCE: Journal of Periodontal Research, (1989) Vol. 24, No. 3, pp. 178-185.
CODEN: JPDRAY. ISSN: 0022-3484.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 1 Sep 1989
Last Updated on STN: 1 Sep 1989

AB Collagen membrane preparations have been manufactured with the aim of enhancing would healing following periodontal surgery. After cross-linking by various processing methods (with ultraviolet radiation or hexamethylenediiso-cyanate) and to various **extents**, **atelocollagen** membranes were applied into dissection sites within palatal gingival tissue. Applied **atelocollagen** was histopathologically compared with applied lyophilized porcine dermis (LPD) and controls in rats, with regard to the time course of healing. The **atelocollagen**-applied group showed more satisfactory regeneration of the epithelium and connective tissue in an artifically created gingival defect than did the control group or the LPD-applied group. Epithelial downgrowth along the root surface was significantly suppressed by the use of **atelocollagen.** In addition, the postoperative inflammatory reaction and foreign body giant cell reaction subsided rapidly after surgery in the **atelocollagen**-applied group. Our results show that the use of **atelocollagen** membrane in periodontal wounds should be the method of choice.

CC Microscopy - Histology and histochemistry 01056
Anatomy and Histology - Surgery 11105
Anatomy and Histology - Regeneration and transplantation 11107
Pathology - Diagnostic 12504
Pathology - Inflammation and inflammatory disease 12508
Pathology - Therapy 12512
Bones, joints, fasciae, connective and adipose tissue - Physiology and biochemistry 18004
Dental biology - Pathology 19006

IT Major Concepts

Dental and Oral System (Ingestion and Assimilation); Pathology; Physiology; Skeletal System (Movement and Support); Surgery (Medical Sciences)
IT Miscellaneous Descriptors
POST-OPERATIVE INFLAMMATORY REACTION HISTOPATHOLOGY ANIMAL MODEL
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L54 ANSWER 31 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 5
ACCESSION NUMBER: 1989:227139 BIOSIS
DOCUMENT NUMBER: PREV198987118756; BA87:118756
TITLE: APPLICATION OF A LOCAL DRUG DELIVERY SYSTEM TO PERIODONTAL THERAPY I. DEVELOPMENT OF COLLAGEN PREPARATIONS WITH IMMOBILIZED TETRACYCLINE.
AUTHOR(S): MINABE M [Reprint author]; UEMATSU A; NISHIJIMA K; TOMOMATSU E; TAMURA T; HORI T; UMEMOTO T; HINO T
CORPORATE SOURCE: DEP PERIODONTOL, KANAGAWA DENT COLL, 82, INAOKA-CHO, YOKOSUKA, KANAGAWA, JPN
SOURCE: Journal of Periodontology, (1989) Vol. 60, No. 2, pp. 113-117.
CODEN: JOPRAJ. ISSN: 0022-3492.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 May 1989
Last Updated on STN: 7 May 1989
AB For the purpose of applying a local drug delivery system to periodontal therapy, **atelocollagen** preparations with immobilized tetracycline (TC) were prepared by modifying the form of the collagen, the concentration of the immobilized TC, and the time of the cross-link process with glutaraldehyde. The course of the TC release form the collagen preparations into an aqueous solution was determined in relation to time. The preparations were also inserted into periodontal pockets, and the amount of TC remaining in the pocket was determined daily. The results obtained were as follows: 1) The degree of drug release could be controlled to some **extent** by adjusting the TC exceeding the effective dose in the gingival crevicular fluid was present in the periodontal pocket even 10 days after the insertion of TC fixed in the cross-linked processed collagen film in the periodontal pockets.
CC Biochemistry studies - General 10060
Pathology - Therapy 12512
Dental biology - General and methods 19001
Dental biology - Pathology 19006
Pharmacology - Clinical pharmacology 22005
Pharmacology - Integumentary system, dental and oral biology 22020
Routes of immunization, infection and therapy 22100
Medical and clinical microbiology - General and methods 36001
Chemotherapy - General, methods and metabolism 38502
IT Major Concepts
Dental Medicine (Human Medicine, Medical Sciences); Dental and Oral System (Ingestion and Assimilation); Infection; Pharmacology
IT Miscellaneous Descriptors
HUMAN ANTIINFECTIVE-DRUG
ORGN Classifier

Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 60-54-8 (TETRACYCLINE)

L54 ANSWER 32 OF 36 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1989:200566 BIOSIS
DOCUMENT NUMBER: PREV198987101470; BA87:101470
TITLE: DIFFERENT CROSS-LINKED TYPES OF COLLAGEN IMPLANTED IN RAT PALATAL GINGIVA.
AUTHOR(S): MINABE M [Reprint author]; KODAMA T; KOGOU T; TAMURA T; HORI T; WATANABE Y; MIYATA T
CORPORATE SOURCE: DEP PERIODONTICS, KANAGAWA DENTAL COLL, 82 INAKO-CHO YOKOSUKA, JAPAN
SOURCE: Journal of Periodontology, (1989) Vol. 60, No. 1, pp. 35-43.
CODEN: JOPRAJ. ISSN: 0022-3492.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 20 Apr 1989
Last Updated on STN: 20 Apr 1989
AB Collagen membrane preparations were manufactured with the aim of enhancing wound healing following periodontal surgery. After crosslinking by various processing methods (with ultraviolet and hexamethylenediisocyanate) and to various **extents**, two types of collagen (**atelocollagen** and tendon collagen) were implanted into a dissection site within palatal gingival tissue. The time course of healing responses was investigated histologically. Collagen implantation was found to accelerate fibrous connective tissue attachment to the root surface and inhibit apical migration of the junctional epithelium. Cross-linked **atelocollagen** was superior in biocompatibility to the other collagen membranes studied.
CC Microscopy - Histology and histochemistry 01056
Biochemistry studies - Proteins, peptides and amino acids 10064
Biophysics - Bioengineering 10511
Anatomy and Histology - Experimental anatomy 11104
Anatomy and Histology - Regeneration and transplantation 11107
Pathology - Comparative 12503
Pathology - Therapy 12512
Dental biology - General and methods 19001
Dental biology - Pathology 19006
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
IT Major Concepts
Clinical Endocrinology (Human Medicine, Medical Sciences); Dental Medicine (Human Medicine, Medical Sciences); Dental and Oral System (Ingestion and Assimilation); Methods and Techniques; Pathology; Physiology
IT Miscellaneous Descriptors
HUMAN EXPERIMENTAL MODEL BIOCOMPATIBILITY HEALING RESPONSE
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L54 ANSWER 33 OF 36 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1986-311723 [48] WPIX
CROSS REFERENCE: 1985-100425 [17]; 1985-106422 [18]; 1985-111858 [19]
DOC. NO. CPI: C1986-135024
TITLE: Slow release preparation of growth promoting or bony metabolism peptide - with collagen, gelatin and/or albumin as carrier protein.
DERWENT CLASS: B04 B05 B07 C03 P32
INVENTOR(S): FUJIOKA, K; SATO, S; TAKADA, Y; YAMAHIRA, Y
PATENT ASSIGNEE(S): (SUMU) SUMITOMO PHARM CO LTD
COUNTRY COUNT: 5
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
AU 8655983	A	19861016	(198648)*		18
JP 61236729	A	19861022	(198649)		
US 4774091	A	19880927	(198841)		
US 5021241	A	19910604	(199138)		
JP 06057658	B2	19940803	(199429)		
US 5385738	A	19950131	(199511)		7

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
AU 8655983	A		AU 1986-55983	19860411
JP 61236729	A		JP 1985-77250	19850411
US 4774091	A		US 1986-846193	19860331
US 5021241	A		US 1988-187443	19880428
JP 06057658	B2		JP 1985-77250	19850411
US 5385738	A	CIP of	US 1984-660044	19841012
		Cont of	US 1986-849968	19860410
		Cont of	US 1990-488531	19900228
			US 1992-844929	19920304

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 06057658	B2 Based on	JP 61236729

PRIORITY APPLN. INFO: JP 1983-193064 19831014; JP
1983-206226 19831101; JP
1983-236994 19831214; JP
1983-236995 19831214; JP
1983-236996 19831214; JP
1985-77250 19850411; JP
1983-220452 19831121
AN 1986-311723 [48] WPIX
CR 1985-100425 [17]; 1985-106422 [18]; 1985-111858 [19]
AB AU 8655983 A UPAB: 19950508

Sustained release preparation comprises a peptide (I) with growth promoting activity or activity relating to bony metabolism, together with a carrier protein from collagen, gelatin and/or albumin. Pref. (I) is growth hormone (GH), growth hormone releasing factor (GRF) or somatomedin (SM) as growth promotor, or calcitonin as bony metabolism active agent.

USE/ADVANTAGE - Useful for treating dwarfism in humans, promoting growth in livestock, promoting lactation, etc. Release can be sustained, avoiding the need for repeated admin.

Dwg.0/1

Dwg.0/1

ABEQ EP 138216 B UPAB: 19930922

A sustained-release preparation for parenteral administration, which comprises interferon as an active ingredient in admixture with a pharmaceutically acceptable biodegradable protein as carrier, said preparation being in the form of powder particles or in the form of a shaped preparation, with the proviso that the form is neither needle-like nor bar-like.

0/1

ABEQ US 4774091 A UPAB: 19930922

Prepn. of slow release pharmaceutical compsn. comprises mixing the active component(s) with an aq. nonotoxic, biodegradable protein soln. (e.g. collagen, **atelocollagen** or gelatin); drying the mixt.; and pressing, extruding or moulding to obtain needle or bar shaped solid compsns.

USE - The process is applicable to a wide range of therapeutic agents, e.g. tissue plasminogen factor, prostaglandins, prostacyclines, hormones, interferones, interleukins, tumour necrosis factor, somatomedines, calcitonine, macrophage activating factor, etc.

ABEQ US 5021241 A UPAB: 19930922

(+12.10.84, 31.3.86-US-660052, 846193) (+1.11.83, 14.12.83(3)-JP-206226, 236994/5/6) (1665TF) Solid sustained release prepn. for injection of implantation consists of an active ingredient and protein carrier in needle or bar-like shape. It is pred. by mixing under aq. conditioned at 5-30 deg.C the active ingredient which is unstable to heat with the biodegradable protein carrier and subjecting mixt. to drying and forming e.g. at R.T. (15-30) deg.C), or by spray-drying or lyophilizing at -50-0 deg.C. Forming is by pressing the powder or pouring into a mould e.g. into a shape suitable for i.m. admin.

Active cpds. pref. include TPA, prostaglandins, prostacyclins, biohormones, interferons, TNF and other cytokines, and interleukins. Also growth hormone and GH releasing factor, somatomedines, calcitonin, macrophage activating factor, migration inhibitory factor and colony stimulating factor. Carriers include collagen, attelocollagen and gelatin.

ADVANTAGE - Gives sustained release for at least 24 hrs. and carrier is absorbed or enzymologised by the body without surgical removal.

ABEQ US 5385738 A UPAB: 19950322

Sustained-release preparation comprises a suspension of a powder in an injectable viscous solvent. The powder comprises an active agent and a biodegradable carrier selected from proteins, polysaccharides and synthetic high molecular cpds. The active agent is pref. indomethacin, bio-hormones, interferons, interleukins, tumour necrosis factor or other cytokines. The carrier is esp. collagen, gelatin, albumin, chitin, polyglycolic acid or polylactic acid.

USE/ADVANTAGE - The active agent is released at an effective level for a long period of time. The compsn. is esp. suitable for medicaments which are unstable to heat and no specific binding agent or heating steps are required in the prepn. of the compsn.

Dwg.0/1

L54 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1985:442660 HCAPLUS
DOCUMENT NUMBER: 103:42660
TITLE: **Sustained-release** injections
INVENTOR(S): Yamahira, Yoshiya; Fujioka, Keiji; Sato, Shigeji; Yoshida, Noboru
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd. , Japan
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 140255	A2	19850508	EP 1984-112313	19841012
EP 140255	A3	19851030		
EP 140255	B1	19910515		
R: CH, DE, FR, GB, LI, SE				
JP 60084213	A2	19850513	JP 1983-193064	19831014
JP 60089418	A2	19850520	JP 1983-197181	19831020
JP 60097918	A2	19850531	JP 1983-206226	19831101
JP 03072046	B4	19911115		
JP 60112713	A2	19850619	JP 1983-220452	19831121
JP 05012328	B4	19930217		
PRIORITY APPLN. INFO.:			JP 1983-193064	19831014
			JP 1983-197181	19831020
			JP 1983-206226	19831101
			JP 1983-220452	19831121

AB A sustained-release injection consists of a suspension of a powder comprising an active ingredient and a biodegradable carrier such as proteins, polysaccharides, gelatins, collagens, etc., in a viscous solvent, e.g., oils, polyethylene glycol [25322-68-3], propylene glycol [57-55-6] silicone oil, and medium-chain fatty acid triglycerides. An aqueous solution of α-interferon (titer 4.9 mU/mL) and 2% atelocollagen is homogeneously mixed with stirring while preventing the occurrence of foams. The mixture is lyophilized and pulverized and suspended in sesame oil to give an oily suspension which shows sustained release properties. The blood levels of the compds. were measured in rabbits after i.m. administration to rabbits. Even after 48 h, the blood levels of 10 U/mL were maintained.

IC ICM A61K009-00
ICS A61K009-22; A61K047-00
CC 63-6 (Pharmaceuticals)
ST **sustained release** injection; collagen
sustained release injection; gelatin **sustained release** injection
IT **Collagens, biological studies**
RL: BIOL (Biological study)
(**atelo-**, **sustained-release** injections containing)
IT Oils
RL: BIOL (Biological study)
(poppy seed, **sustained-releasing** injections containing)
IT Oils
RL: BIOL (Biological study)
(sesame, **sustained-release** injections containing)
IT Castor oil
Collagens, biological studies
Corn oil

Cottonseed oil
Gelatins, biological studies
Hormones
Interferons
Olive oil
Peanut oil
Polysaccharides, biological studies
Prostaglandins
Proteins
Siloxanes and Silicones, biological studies
RL: BIOL (Biological study)
(**sustained-release** injections containing)

IT **Pharmaceuticals**
(injections, **sustained-release**, biodegradable carriers for)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin, **sustained-release** injections containing)

IT Glycerides, biological studies
RL: BIOL (Biological study)
(medium-chain, **sustained-release** injections containing)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(tumor necrosis factor, **sustained-release** injections containing)

IT Interferons
(α-, **sustained-release** injections containing)

IT 52-24-4 53-86-1 57-55-6, biological studies 1404-00-8 11056-06-7D, derivs. 23214-92-8 25322-68-3 97330-37-5
RL: BIOL (Biological study)
(**sustained-release** injections containing)

L54 ANSWER 35 OF 36 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1985-100425 [17] WPIX
CROSS REFERENCE: 1985-106422 [18]; 1985-111858 [19]; 1986-311723 [48]; 1988-149707 [22]
DOC. NO. CPI: C1985-043388
TITLE: Sustained release compsn. of indomethacin, interferon - or 4-carbamoyl-imidazolium-5-ol ate, in biodegradable carrier, e.g. collagen.
DERWENT CLASS: B04 B05 B07 C03 P32
INVENTOR(S): FUJIOKA, K; SATO, S; YAMAHIRA, Y; YOSHIDA, N; YAMASHIRA, Y; TAKADA, Y
PATENT ASSIGNEE(S): (SUMU) SUMITOMO PHARM CO LTD; (SUMO) SUMITOMO CHEM CO LTD
COUNTRY COUNT: 11
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 138216	A	19850424	(198517)*	EN	27
R: CH DE FR GB LI SE					
JP 60084213	A	19850513	(198525)		
JP 60089418	A	19850520	(198526)		
JP 60097918	A	19850531	(198528)		
US 4855134	A	19890808	(198939)		
JP 03072046	B	19911115	(199150)		
US 5081156	A	19920114	(199206)		
EP 138216	B1	19930107	(199302)	EN	7
R: CH DE FR GB LI SE					
DE 3486029	G	19930218	(199308)		

US 5385738 A 19950131 (199511) 7

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 138216	A		EP 1984-112312	19841012
JP 60084213	A		JP 1983-197181	19831020
JP 60089418	A		JP 1983-193064	19831014
JP 60097918	A		JP 1983-206226	19831101
US 4855134	A		US 1986-855387	19860424
JP 03072046	B		JP 1983-206226	19831101
US 5081156	A		US 1989-358157	19890530
EP 138216	B1		EP 1984-112312	19841012
DE 3486029	G		DE 1984-3486029	19841012
			EP 1984-112312	19841012
US 5385738	A	CIP of	US 1984-660044	19841012
		Cont of	US 1986-849968	19860410
		Cont of	US 1990-488531	19900228
			US 1992-844929	19920304

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 3486029	G	Based on	EP 138216

PRIORITY APPLN. INFO: JP 1983-193064 19831014; JP 1983-197181 19831020; JP 1983-206226 19831101; JP 1983-220452 19831121; JP 1983-236996 19831214; JP 1985-77250 19850411

AN 1985-100425 [17] WPIX

CR 1985-106422 [18]; 1985-111858 [19]; 1986-311723 [48]; 1988-149707 [22]

AB EP 138216 A UPAB: 19950508
Sustained release compsn. comprises indomethacin (I), interferon (II) or 4-carbamoyl-imidazolium-5-olate (III) as active ingredient, and a biodegradable carrier. The carrier may be a protein, polysaccharide or synthetic high mol. cpds. It is pref. collagen, **atelocollagen**, gelatin, albumin or chitin.

USE/ADVANTAGE - Compsns. may be administered parenterally giving maintained levels of the active ingredient in the blood for long periods. The carrier does not accumulate in the body. (I) is a non-steroidal antirheumatic agent with local antiinflammatory activity. (II) is an antiviral and antitumour agent. (III) is an antitumour agent, which inhibits purine synthesis.

Dwg.0/4

Dwg.0/4

ABEQ EP 138216 B UPAB: 19930925
A sustained-release preparation for parenteral administration, which comprises interferon as an active ingredient in admixture with a pharmaceutically acceptable biodegradable protein as carrier, said preparation being in the form of powder particles or in the form of a shaped preparation, with the proviso that the form is neither needle-like nor bar-like.

0/1

ABEQ US 4855134 A UPAB: 19930925
Sustained-release prepn. comprises interferon, as an active ingredient, and collagen, as a carrier. The prepn. is in the form of powder particles

suspended in a viscous solvent suitable for injection; or is in the form of a shaped prepn. suitable for use as an injection in a solid state or for implanting into a body.

Pref. the interferon is alpha-interferon. Pref. the new prepn. is prepd. by a) mixing interferon and collagen to form a liq. mixt.; and drying the resultant mixt.

ADVANTAGE - New prepn. can maintain the desired level of active ingredient in blood or in a lesional region for a long time.

ABEQ US 5081156 A UPAB: 19930925

Sustained-release compsns. comprise indomethacin or its salt as active ingredient and collagen as carrier, the compsns. being prepd. by: (a) mixing the components to form a liq. mixt. and (b) drying the mixt. without heat treatment. Pref. the compsns. contain 0.5-500 mg of indomethacin or its salt per dosage unit. Pref. they also contain a small amt. of gelatin.

USE/ADVANTAGE - As antiinflammatory agents vs. local inflammation while avoiding undesirable side effects on the CNS and peptic organs.

ABEQ US 5385738 A UPAB: 19950322

Sustained-release preparation comprises a suspension of a powder in an injectable viscous solvent. The powder comprises an active agent and a biodegradable carrier selected from proteins, polysaccharides and synthetic high molecular cpds. The active agent is pref. indomethacin, bio-hormones, interferons, interleukins, tumour necrosis factor or other cytokines. The carrier is esp. collagen, gelatin, albumin, chitin, polyglycolic acid or polylactic acid.

USE/ADVANTAGE - The active agent is released at an effective level for a long period of time. The compsn. is esp. suitable for medicaments which are unstable to heat and no specific binding agent or heating steps are required in the prepn. of the compsn.

Dwg.0/1

L54 ANSWER 36 OF 36 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1981-82496D [45] WPIX
TITLE: Drug carrier material - comprises atelo-collagen which is free of antigenicity.
DERWENT CLASS: B07
PATENT ASSIGNEE(S): (KOKE) KOKEN KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 56122317	A	19810925	(198145)*		6

PRIORITY APPLN. INFO: JP 1980-25806 19800229
AN 1981-82496D [45] WPIX
AB JP 56122317 A UPAB: 19930915

Carrier for drugs (e.g. anticancer agents, antibiotics, etc.) comprises **atelocollagen** free of antigenicity.

Preparation comprises selectively digesting and removing telopeptide present at terminal portions of collagen mols. by a protease to produce atelo-collagen free of antigenicity and mixing the **atelocollagen** with drug followed by moulding the mixture into prescribed form.

Atelocollagen shows biological characteristics such as freeness from rejection or allergy reaction, good affinity to living tissues, etc. Additionally, it shows affinity to various drugs because of its amino, guanidyl, carboxyl, hydroxyl and peptide gps. and temporarily retains drug and gradually releases it when adhered to living body or

buried into tissues. By introducing crosslinking to **atelocollagen** , the size of the collagen matrix network can be controlled, and rate of release can be decreased due to inhibited swelling of the matrix with water.

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